47 percent by flexography, 1 percent by gravure, and the remaining by other methods. Applying these proportions to the RTI model for complex printing tasks with four or more color changes, NDMA derived a label printing cost of $3,458 per SKU for an average OTC drug product and concluded that this result verified its estimate of $4,039 per SKU (without scrap).

The agency agrees that the cost data used in FDA's economic analysis of the proposed rule were not drawn from a random sample, although they were supplied by sources familiar with the OTC drug industry, including smaller and private label manufacturers. FDA notes, however, that the survey underlying the NDMA cost estimates was likewise not based on a random sample of manufacturers. While NDMA member firms include a range of large, small, brand-label, and private-label manufacturers, many smaller firms do not belong to NDMA. Indeed, NDMA indicates that its 74 members (which may represent less than 20 percent of all OTC drug manufacturers), account for 90 to 95 percent of all OTC drug sales. A survey limited to this membership necessarily over-represents large manufacturers of nationally branded products and under-represents smaller manufacturers of regionally branded products.

Following review of the survey data provided by NDMA, FDA concludes that NDMA's figures overstate the industry average cost of redesigning OTC drug labels. For example, the survey reports unreasonably large differentials between branded and private label manufacturers, with survey costs for branded SKU's from 3 to 40 times greater than those for private label SKU's. For graphics development (directions for studio, draft/mock-ups, review, and concurrence), the average SKU cost reported was $6,215 for branded and $291 for private label products. Assuming an hourly wage rate of $40 for branded and private product personnel, manufacturers of branded products spend 155 hours per SKU on this function compared to 7 hours by private labelers. For separations (color mock-ups created and reviewed), the survey reported the per SKU cost for branded and private label companies at $3,210 and $82, respectively, almost a 40-fold difference. The agency acknowledges that large manufactures of nationally branded products involve more personnel in decision making and may use higher quality packaging materials. Nevertheless, in

view of the substantial degree of market competition in this industry, private labelers typically package goods to resemble the competing national brand. Moreover, while questioning the size of the reported range, FDA could not review the basis for NDMA's estimates, because the supporting data, such as the number of labor hours or labor costs used in its calculations, were not submitted.

Furthermore, while the proposed rule required manufacturers to reformat the information panels, the NDMA survey instructed respondents to include the cost of changing all labeling, including certain promotional materials. Thus, some manufacturers may have reported costs for developing new product identities, advertising campaigns, etc. Also, survey respondents were asked to estimate the cost to redesign only one SKU, which ignores both learning curve and economy of scale effects. For the most part, the same industry personnel are responsible for copy and layout decisions for numerous product lines and SKU's. Moreover, FDA does not agree that the RTI model necessarily validates NDMA's redesign cost estimate. The portion of the RTI model used by NDMA was developed to estimate the cost of printing food labels, which are often considerably larger than OTC drug labels.

NDMA's recent estimate also differs from the average cost of $7,900 per SKU submitted by the Cosmetic, Toiletry, and Fragrance Association to change a drug-cosmetic label (Ref. 27). OTC drug-cosmetics are generally considered to have more expensive labeling than OTC drugs alone, because they compete with other elaborately packaged cosmetic products.

To finalize its estimate of the average cost of redesigning an OTC drug label, FDA considered several approaches. First, the agency maintained its initial estimating methodology, but adjusted the estimated unit cost per SKU. Based on all available information, FDA concludes that the cost of redesigning nationally branded products manufactured by large companies ranges from $5,000 to $15,000 per SKU. The cost to redesign regional or low sales volume brands of smaller manufacturers is considerably less, ranging from about $1,000 to $8,000 per SKU. The cost to redesign labels for private label brands is smaller still, but approximates FDA's original estimate

of $1,000 and NDMA's survey estimate of $1,261 per SKU. Accordingly, to calculate a final estimate, the agency divided OTC drug products into three classes: (1) Branded products manufactured by large NDMA member companies, with a midpoint cost estimate of $10,000 per SKU; (2) branded products manufactured by smaller companies, with a mid-point cost estimate of $4,500 per SKU; and (3) private label products, assumed to cost $1,261 per SKU, as reported by NDMA.

The agency used its original estimate of the SKU distribution, which indicated that about 30 percent of all OTC drug SKU's are branded, and the NDMA member survey to determine costing weights to apply to each industry sector. Respondents to NDMA's survey reported that they account for about 4,000 branded SKU's, which amount to 15 percent of all branded SKU's. As these survey respondents comprise almost half of NDMA's membership, FDA assumed that branded products of all NDMA members may account for about 30 percent of all branded SKU's, or approximately 10 percent of all affected SKU's (30 percent branded x 30 percent NDMA members). The remaining branded products, therefore, account for 20 percent of all affected SKU's, and the private label products account for the remaining 70 percent. This calculation results in a weighted average cost of $2,783 (without scrap) to redesign a label (i.e., ($10,000 x 10 percent)+($4,500 x 20 percent)+($1,261 x 70 percent)), a figure higher than the prior FDA estimates but below the NDMA survey estimate of $4,039.

A second approach was developed by the Eastern Research Group, Inc. (ERG), a private economics consulting firm under contract to FDA. ERG developed its model based on data collected during site visits to several large and small drug companies and through discussions with other industry consultants (Ref. 28). ERG assumed a more complex distribution of various types of SKU's among firms of different sizes and included specific cost variables for regulatory affairs, art/graphics, manufacturing changes, and inventory losses by firm size (by employment), firm type (branded or private label), and type of label changed (carton, container, etc.). Under ERG's model,

the estimated weighted average cost of label redesign (without scrap) is $1,210 per SKU (Ref. 28).

Because the OTC industry is so diverse and the relevant cost data are so limited, no single model or single estimate can be viewed as definitive. Nevertheless, the agency continues to believe that its overall approach represents a rational basis for estimating the redesign costs associated with this rule. The agency in its proposed analysis arrived at an estimate of $2,070 per SKU (without a PDP adjustment). That figure, when revised to take into account certain data from the NDMA survey, is increased to $2,783 per SKU. ERG employed a more complex model and arrived at a figure of $1,210 (or half that of FDA), while NDMA arrived at a weighted average of $4,039 (or twice that of FDA). Given this spread, and given the agency's concerns about NDMA's methodology and input data, the agency is adopting the revised figure of $2,783 as its base average cost estimate. The agency acknowledges that it has adopted a conservative figure, relative to that derived by ERG. However, nothing in the ERG model, or in the NDMA model, suggests that FDA should discard its methodology or its assumptions for estimating unit costs.

ii. *Principal display panel.* In its original analysis, FDA assumed that the PDP need not be altered and therefore adjusted its unit cost estimate for branded products downward by 50 percent. NDMA argued that this correction was inappropriate as it failed to account for many commonly used labeling and packaging configurations. NDMA pointed out that, with the exception of labels with separate front and back panels, all PDP's must be reprinted when the information panel is changed. Based on a poll of 7-member companies, NDMA estimated that about 90 percent of all OTC drug SKU's require the PDP to be reprinted when changes are made to the information panel.

The fact that the PDP needs to be reprinted when the information panel is changed does not mean that it has to be redesigned. For the majority of labels, the PDP and information labeling are printed as a single label, with one printing plate required for each of the colors used. For many products, only one or two colors will be changed on the information panel to accommodate

the new requirements; consequently, only those plates would need to be redesigned, the others could be reused or simply copied at significantly reduced cost. Nevertheless, the agency acknowledges that many manufacturers would, at the time of redesigning the information panel, also make incremental changes to the PDP. Therefore, the agency has adopted the NDMA position and eliminated any downward PDP adjustment from its calculation of the cost of the final rule.

iii. *Scrap*. NDMA also argued that the cost of scrapping unused inventory should be included as a regulatory cost. Based on its survey, it estimated that scrap labeling inventory adds about $1,000 to the weighted redesign cost per SKU ($2,968 per SKU for higher cost firms and $576 per SKU for lower cost firms), raising its average unit cost estimate to about $5,000. NDMA declared this a conservative estimate that would underestimate the cost of scrap label inventory if the implementation date were less than 2 years.

FDA agrees that some scrap label inventory loss is inevitable when label changes are made, but notes that the longer the implementation period the easier it is for manufacturers to minimize the cost. The final rule allows either a 2- or 3-year implementation phase (depending on sales volume), which is sufficient time to minimize inventory losses. Because the NDMA survey question failed to state the length of the phase-in period, the survey response cannot be considered reliable. Nonetheless, because a better estimate of the average scrap cost is not available, FDA accepts NDMA's figures, but adjusts the weighting to 10 percent for the higher cost firms and 90 percent for the lower cost firms, for a weighted average of $800. This weighting is based on the assumption that both small brand name manufacturers and private label manufacturers have less expensive labels and smaller inventories than large brand-name companies. The consideration of scrap, therefore, raises FDA's weighted average design cost estimate to approximately $3,600 per SKU.

iv. *Administrative costs*. NDMA suggested that the agency also include administrative costs in its calculation of the cost to redesign the label. NDMA provided no estimate of these costs, but noted that there would be a burden to manufacturers to manage the additional required redesign of labels.

FDA agrees that the rule will impose administrative costs, but concludes that these costs are adequately accounted for in the previous estimates. OTC drugs are highly regulated products and manufacturers are expected to have regulatory personnel on staff or consultants available to address compliance matters. The complexity of the rule is not unusual compared to other OTC drug regulations and the requirements will be clear to graphics design and regulatory personnel. Moreover, the rule is expected to receive widespread publicity when issued and most OTC drug firms belong to trade associations or have access to trade publications that provide additional sources of information. Because the rule permits a 2- to 3-year implementation period, FDA continues to believe that managing the label changes will not impose burdens beyond the costs included in the agency's estimate.

b. *Methodology for calculating economic impact.* NDMA disagreed with the methodology the agency used to calculate the economic impact of the proposed rule for two reasons: (1) FDA treated the cost to redesign as a financed rather than an expensed cost and calculated the impact using an amortized cost rather than a net present value, and (2) FDA treated label redesign as an accelerated change rather than an additional change.

i. *Economic versus accounting costs.* NDMA asserted that FDA used an incorrect valuation method to assess the economic impact of the rule, because the agency's valuation of amortized lost label life incorrectly implies that the costs of label redesign are financed costs, rather than sunk costs expensed in the year they incur. According to NDMA, the proper approach is not to amortize, but to calculate the net present value of the incremental costs of label redesign.

FDA does not agree that the amortization of lost label life is inappropriate. Executive Order 12866 charges Federal agencies to determine the economic cost of its rules, but such costs are not necessarily identical to financial costs, as interpreted by accounting convention. According to the U.S. Office of Management and Budget (Ref. 29), the preferred measure for economic analyses is ''the opportunity cost' of the resources used or the benefits forgone as a result of the regulatory action.'' Whether firms expense label design costs in the year they occur is largely irrelevant to

the proper calculation of economic costs, i.e., the opportunity cost of the rule. Moreover, FDA's calculation yields results that are identical to those obtained through a net present value approach. To derive its results, FDA estimated a net present value and then, for ease of exposition, converted this figure into an equivalent stream of annual costs.

ii. *Additive versus accelerated costs.* The primary reason that NDMA's methodology produces substantially higher costs than FDA's estimate is that NDMA's approach assumes a ''market driven'' label cycle that is independent of the design changes required by the rule. For example, if the average lifetime of a particular label type is 3 years and a design change costs $3,000 per SKU, both FDA and NDMA agree that a 2-year phase-in would allow two-thirds of the labels to be replaced under normal business conditions without additional costs (assuming no package size changes). FDA's methodology, however, also assumed that the remaining one-third of the labels lose only 1-year of their expected lifetime, so that the economic cost (ignoring any discounting adjustment) would be $1,000 per SKU (1/3 x $3,000) for one-third of these SKU's. This approach, however, implicitly assumes that the label design cycle would resume at a 3-year interval, so that the next voluntary label redesign, on average, would not occur until 3 years after the mandated change.

In contrast, NDMA argues that voluntary label redesign occurs in response to external ''market driven'' factors that would be independent of this mandated change. According to NDMA, such redesigns are to change product attribute copy; change graphics; add litigation-driven warnings; delete ''new'' flags after 6 months; add multilingual labeling; change labeling information, such as manufacturer, distributor, or inactive ingredient; or add or change SKU's in a product line. NDMA contends that, because the mandated changes required by this rule would not affect the underlying ''market driven'' design cycle, the full cost of the redesign, rather than just the value of the remaining life of the former label, measures the economic cost of the regulation.

With respect to the previous numerical example, NDMA's methodology implies that those labels that were redesigned in year 2 for regulatory reasons would, on average, be redesigned

again in year 3 for ''market driven'' reasons. (FDA would assume that the labels that had to be redesigned in year 2 would not, on average, be redesigned again until year 5.) NDMA's methodology, therefore, would calculate the economic cost at about $3,000 per affected SKU, compared to FDA's estimate of about $1,000.

The agency does not dispute the theoretical possibility of NDMA's argument. If ''market driven'' reasons for label adjustments always compelled an immediate response, companies could not coordinate voluntary label updates with mandatory label redesign; the regulatory cost for each affected label, therefore, would be the full cost of the design change. However, FDA does not agree that such abrupt shifts in marketing strategies are the industry norm. Many of the examples of ''market driven'' label changes NDMA cited are for exactly the kind of incremental adjustments that would be deferred and consolidated in a major redesign effort. For example, the demand for most changes to product attribute copy or graphics mounts gradually in response to shifting advertising and marketing styles. Once changed, such modifications postpone the need for future change. Revisions for litigation-driven warnings are less common events that would be expected to have a small effect on industry averages. According to the RTI study (Ref. 28), line copy changes or changes affecting just one color are minor changes that, in most cases, are made without the assistance of a label artist and cost one-sixth the cost of a four-or-more color change. Such minor adjustments would not be expected to alter the underlying design cycle.

The agency finds it more likely that the demand for most major label changes is a steadily increasing function of the time that has elapsed since the last labeling revision and that manufacturers continually refine marketing techniques and strategies. As most companies will find it cost-effective to complete these incremental labeling changes concurrently with the mandatory redesign required by this rule, FDA's revised analysis maintains the assumption that the current labeling change cycle will continue unaltered. Moreover, it is important to note that the agency's decision not to exclude PDP design costs is based on its finding that incremental style modifications

accompany mandated changes. If firms would not bundle incremental style changes with the mandated changes, the PDP design costs should be subtracted from the regulatory cost estimate.

c. *Cost of increasing size of packages and/or labels.* Several comments objected to FDA's assumption that the proposed rule would require few changes to the size or configuration of OTC drug packages or labels. NDMA reported that its survey indicated that 33 percent of branded and 95 percent of private label SKU's could not accommodate the proposed label format. NDMA estimated that exemption petitions would be filed for 33,500 SKU's, that 32,600 SKU's would alter package configuration at a cost of over $1 billion, and that about 15,500 SKU's would be removed from the market. While not including administrative costs for feasibility studies to determine cost-effective packaging and labeling configurations, NDMA stated that they would be large. One manufacturer suggested that a new packaging line to accommodate a label change for just one product line would result in a one-time equipment expenditure of about $2.5 million (including equipment, installation, validation, depreciation of old equipment, facility renovation, and inventory loss) and recurring costs of almost $500,000 for the more expensive labeling.

The previously mentioned projections greatly overestimate the percentage of SKU's that will not be able to accommodate the new format and the cost of increasing the size of the labeling, where necessary. In particular, the assertion that 95 percent of private label SKU's could not accommodate the proposal requirements is difficult to understand, as the vast majority of private label OTC drug products are packaged almost identically to the leading branded products for competitive reasons. Moreover, the agency carefully reviewed labels submitted as examples of those that would not fit the proposed format and found that many could, in fact, accommodate the final rule without a change in label or package size.

FDA also questions the methodology for calculating the costs of package size changes. Although details of these calculations were not submitted, it appears that NDMA estimated the cost of purchasing or modifying equipment by multiplying the unit costs by the number of affected SKU's, with no allowance for multiple SKU's packaged on a given production line, or for the

widespread usage of contract packagers. Although agreeing that such factors should be considered when determining costs, NDMA nonetheless assumed substantial equipment requirements for each SKU. Moreover, NDMA does not differentiate between the costs of branded and private label manufacturers. Most private label products are manufactured by firms that produce hundreds of SKU's on the same equipment, as most packaging machines can accommodate a spectrum of changes with only minor modification or retooling. As firms will choose the most cost-effective means of implementing package changes, only in rare cases, or when equipment is already obsolete, should the rule lead to the purchase of new equipment.

For some small SKU's, the impact of this rule will be moderated by the more flexible leading and formatting provisions in the final rule and the modified small package format allowed in 201.66(d)(10). FDA further believes that any reduced consumer choice, should a small package product not be able to meet the new requirements, will be relatively insignificant because most manufacturers offer products in more than one package size.

To respond fully to the estimates offered by NDMA, FDA asked its economics consultant, ERG, to survey (Ref. 28) all of the OTC drug products found on the shelves in three retail outlets in the Boston area. These outlets included: (1) A large pharmacy chain, (2) an independent pharmacy, and (3) a convenience store. ERG examined each of the 2,689 distinct SKU's found on the store shelves, and recorded data on the package size and type, the available labeling space, and the font size. ERG then compared these data to generic mock-ups of the revised monographs to estimate the percent of the SKU's that might need to increase the size of either the label or package. ERG also estimated the amount of the additional space needed to accommodate the new format for those SKU's that lacked sufficient labeling surface area, using an expansion factor to derive estimates for SKU's for which no adequate mock-ups were available.

The results of the survey are shown by type of package in Table 3 of this document. The vast majority of SKU's, 92 percent, have sufficient labeling space to accommodate the revised format. Of these, 16 percent will require some reconfiguration of the current information

presentation, such as moving, reducing, or eliminating certain marketing information. Another 1.7 percent of the SKU's would increase the size of their label to accommodate the new format and 6.4 percent either would not fit or were indeterminate (too close to call) and, thus, might require a new packaging configuration. (SKU's were judged indeterminate when the available labeling area was within 5 square centimeters of the required area.)

TABLE 3.—FINDINGS FOR 6.0-POINT FONT, CONDENSED TYPE ALLOWED[1]

Labeling outcome	Percent of SKU's
Revised label can fit using existing area allotted for regulatory information	75.9
Revised label fits if area allotted for regulatory information is increased	16.0
Revised label fits if expanded on existing container	1.7
Revised label will not fit	4.5
Indeterminate	1.9
Total	100

[1] Horizontal width of the characters reduced by approximately 20 percent while the vertical height of the characters is unchanged.

To evaluate the estimate of reconfiguration costs (i.e., changes to the size of the labeling or packaging) presented in the comments, ERG considered several options for packaging changes, including adding a carton (if not already present), adding a fifth panel, increasing the size of the packaging, or switching to a nonstandard form of labeling such as peel-back or accordion labels (Ref. 28). Where applicable, the costs for changing a container size included container inventory loss, adjustment of the packaging line, and stability testing. The estimated packaging change costs varied with the option chosen (for example, adjustment or retooling of existing machinery versus the purchase of new equipment), although the lower cost options had a higher probability of selection. ERG also considered the recurring annual costs that would be associated with the need for larger labels or packages. A detailed description of ERG's assumptions, calculations, and unit costs is presented in the full report.

4. Total Incremental Costs

The costs of labeling redesign apply only to products covered by final OTC drug monographs or applications. Currently there are about 39,310 SKU's in this category (see Table 2 of this document). No redesign costs are assigned to the remaining 59,330 SKU's because the 6-year implementation period for these products will allow manufacturers to incorporate the design

changes in their usual redesign cycle. Using a weighted average cost to redesign a label of $3,600 per SKU and assuming labels are redesigned voluntarily every 2, 3, or 6 years, the total incremental costs for redesigning labeling using the methodology discussed earlier is $19.4 million.

Reconfiguration costs apply to those products that cannot accommodate the small package format allowed in § 201.66(d)(10). These costs include the one-time cost to increase labeling size (the label or package, where applicable) to accommodate a minimum 6.0 condensed font, plus the recurring cost of producing larger labeling. Because these costs are applied to this rule regardless of the monograph status of the product, all 98,639 SKU's are potentially subject to label reconfiguration costs; 39,310 within 2 years of the effective date of this final rule, the remaining 59,330 within 6 years of the effective date of this final rule. The estimated reconfiguration costs amount to $38.1 million in one-time costs and $11.5 million in annual recurring costs. The latter reflects the incremental increases in labeling or packaging materials to accommodate the format requirements.

Table 4 of this document presents FDA's estimate of the one-time and annual recurring costs and the total annualized cost by compliance activity. The total one-time costs of $57.5 million include $19.4 million for label redesign and $38.1 million for packaging changes. The annual costs are $11.5 million. The total annualized cost to industry (using a 7 percent discount rate) is estimated at $18.4 million. The cost to individual firms will vary with the number of SKU's, the type of changes needed, and the timing of the changes.

TABLE 4.—TOTAL INDUSTRY COMPLIANCE COSTS

Activity	One-Time ($Million)	Annual ($Million)	Total Annualized
Label redesign	19.4	NA	1.4
Packaging	38.1	11.5	17.0
Total	57.5	11.5	18.4

These estimates may overstate the costs attributable to this rule. First, reconfiguration costs will be reduced to the extent that companies opt to eliminate some smaller packaging sizes within a product line. In these instances, however, consumers will bear some of the added costs. Second, the recent amendment to section 502(e) of the act under FDAMA requires that OTC drug

manufacturers list the inactive ingredients in their labeling. The ERG retail outlet survey (Ref. 28) found that about 7 percent of the SKU's currently do not include inactive ingredients on their labels. Some of these products may need larger label or package sizes irrespective of this rule.

D. Small Business Impact

Manufacturers and those entities that engage in the relabeling of OTC drug products will be required to redesign the labeling of their products to comply with this rule. Census data provide aggregate industry statistics on the number of manufacturers for Standardized Industrial Classification Code 2834, Pharmaceutical Preparations, by establishment size, but do not distinguish between manufacturers of prescription and OTC drugs. Over 92 percent of the roughly 700 establishments and over 87 percent of the 650 firms in this sector have fewer than 500 employees. The Small Business Administration (SBA) considers firms with fewer than 750 employees in this industry to be small, but the U.S. Census size categories do not correspond to the SBA designation. An alternative data source, IMS, identified roughly 400 firms as manufacturers of OTC drug products. Using the SBA size designation of 750 employees, about 70 percent of the 400 affected manufacturing firms would be considered small.

This regulation will affect the information content and format associated with OTC drug product labeling. Firms that manufacture or relabel OTC drug products will need to change the information panel for each affected product and may need to increase the size of the packaging or labeling for a few SKU's. These costs will be mitigated, however, by the several year implementation period, which will permit many of these changes to be coordinated with those labeling changes conducted in the normal course of business. OTC drug products subject to new drug and ANDA's will need to submit revised labeling to the agency in accordance with § 314.70. This is a standard procedure that companies routinely follow for labeling changes. The final rule will not require new reporting and recordkeeping activities. Therefore, no additional professional skills are necessary.

The economic impact of this rule on small firms is particularly difficult to measure, because published financial data do not distinguish between firms manufacturing mostly OTC drugs and firms manufacturing mostly prescription drugs. ERG adopted Census data on firm size and revenue for SIC 2834, Pharmaceutical Preparations, and assumed 400 manufacturers of OTC drug products to derive the figures in Table 5 of this document. These data indicate that if 90 percent of the OTC drug product firms meet the SBA size criteria for small businesses, the annualized industry cost attributed to small businesses would amount to $12.3 million out of the total $18.4 million. If revenues of small OTC drug product manufacturers are similar to those of all small manufacturers in SIC 2834, these costs represent only 0.17 percent of small business OTC drug revenues.

TABLE 5.—SMALL BUSINESS IMPACT

	OTC Manufacturing Total	OTC Small Business Total
Firms	400	357
Establishments	478	374
Employees	86,849	18,942
Average employees per firm	217	53
Percentage of total small business employment	NA	100%
Receipts ($000)	$42,363,000	$7,411,000
Receipts per firm ($000)	$106,000	$21,000
Total SKU's affected	98,639	65,792
As percentage of all SKU's	100%	66.7%
Total annualized compliance costs ($ millions)	$18.4	$12.3
Total annualized compliance costs as percentage of annual revenues	0.0004	0.0017

These calculations, however, assume that small businesses can finance the one-time outlays over time. In fact, some small firms may have difficulty raising the funds. FDA finds that, on average, the incremental one-time cost per SKU is about $600 ($57.5 million ÷ 98,639 SKU's). If a small firm manufactures 10 or 20 SKU's, it might need to raise from $6,000 to $12,000 within the permitted implementation period. In view of the figures developed for Table 5 of this document, which imply that the annual revenue per SKU averages about $100,000 for small businesses, such one-time outlays should be manageable for most small firms.

The agency has taken a number of steps to minimize the impact on small entities, including: (1) A 2- to 6- year implementation period to allow the sale of existing product inventories and to permit coordination of required labeling changes with routine industry-initiated labeling changes, (2) a modified format for small packages, (3) an additional phase-in year for OTC drug products

covered by a final monograph or an approved drug application if yearly sales are less than $25,000, and (4) coordination of the FDAMA requirement for listing inactive ingredients with the implementation of this rule. These provisions will provide additional flexibility and cost savings for small entities.

E. Alternatives

The major regulatory alternatives considered included various implementation periods and graphics features, including font sizes and print types. As shown in Table 6 of this document, redesign costs for the 39,310 SKU's with a final monograph decrease substantially with longer

implementation periods for products covered by final monographs or approved drug applications. One-time costs for a 1-year implementation period would be about $59.1 million. A 2-year implementation period reduces this figure to $27 million and a 3-year period to $11.9 million. The selected alternative, which includes the 2-year implementation period, but permits a third year for products with low volume sales, reduces these redesign costs to $19.4 million. The agency believes this implementation period will provide substantial relief to industry while achieving important consumer safety and use goals in a timely manner.

TABLE 6.—EFFECT OF IMPLEMENTATION PERIOD ON REDESIGN COSTS

Implementation Period for Final Monographs	Cost ($ Millions)	Redesign Cost With 1 Additional Year for Low Volume Products ($ Millions)
1 year	59.1	46.9
2 years	27.0	19.4
3 years	11.9	8.9

FDA also considered alternative requirements for minimum font sizes and print types. Table 7 of this document presents, for several alternatives, ERG's estimates of the percent of SKU's with current labels too small to fit, the one-time costs for labeling reconfiguration, and the recurring label, carton, and container costs, under varied font size and print requirements. The annualized cost for a minimum 6.0 font but not condensed type (i.e., the horizontal width of the characters reduced approximately 10 to 20 percent while the vertical height of the characters is unchanged) requirement would be $25 million. The final rule allows condensed print, which reduces this cost to $17 million. The agency considered but rejected labeling with smaller than 6-point type size because of the readability issues associated with such labeling.

TABLE 7.—EFFECT OF PRINT REQUIREMENTS ON LABELING RECONFIGURATION COSTS

Minimum Font Size, Print Type Required	Percent of SKU's That Cannot Fit or Are Indeterminate	One-Time Packaging Reconfiguration ($ Millions)	Recurring Incremental Label, Carton and Container Materials ($ Millions)	Total Annualized Packaging Cost ($ Millions)
6.0, not condensed	9.5	45.9	18.3	25.0
6.0, condensed allowed	6.4	38.1	11.5	17.0
4.5, not condensed	3.4	21.0	5.1	8.2
4.5, condensed allowed	2.3	14.0	3.4	5.4

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List of Subjects

21 CFR Part 201

Drugs, Labeling, Reporting and recordkeeping requirements.

21 CFR Part 330

Over-the-counter drugs.

21 CFR Parts 331, 341, 346, 355, and 358

Labeling, Over-the-counter drugs.

21 CFR Part 369

Labeling, Medical devices, Over-the-counter drugs.

21 CFR Part 701

Cosmetics, Labeling, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act, and under authority delegated to the Commissioner of Food and Drugs, 21 CFR parts 201, 330, 331, 341, 346, 355, 358, 369, and 701 are amended as follows:

PART 201—LABELING

1. The authority citation for 21 CFR part 201 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 358, 360, 360b, 360gg–360ss, 371, 374, 379e; 42 U.S.C. 216, 241, 262, 264.

2. Section 201.63 is amended by revising the section heading, the first sentence in paragraph (a), and paragraph (e) to read as follows:

§ 201.63 Pregnancy/breast-feeding warning.

(a) The labeling for all over-the-counter (OTC) drug products that are intended for systemic absorption, unless specifically exempted, shall contain a general warning under the heading ''Warning'' (or ''Warnings'' if it appears with additional warning statements) as follows: ''If pregnant or breast-feeding, ask a health professional before use.'' [first four words of this sentence in bold type] * * *

* * * * *

(e) The labeling of orally or rectally administered OTC aspirin and aspirin-containing drug products must bear a warning that immediately follows the general warning identified in paragraph (a) of this section. The warning shall be as follows:

''It is especially important not to use'' (select ''aspirin'' or ''carbaspirin calcium,'' as appropriate) ''during the last 3 months of pregnancy unless definitely directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery.''

3. Section 201.64 is amended by revising the last sentence in paragraph (b) to read as follows:

§ 201.64 Sodium labeling.

* * * * *

(b) * * * The sodium content per dosage unit shall follow the heading ''other information'' as stated in § 201.66(c)(7) of this chapter.

4. Section 201.66 is added to subpart C to read as follows:

§ 201.66 Format and content requirements for over-the-counter (OTC) drug product labeling.

(a) *Scope*. This section sets forth the content and format requirements for the labeling of all OTC drug products. Where an OTC drug product is the subject of an applicable monograph or regulation that contains content and format requirements that conflict with this section, the content and format requirements in this section must be followed unless otherwise specifically provided in the applicable monograph or regulation.

(b) *Definitions*. The following definitions apply to this section:

(1) *Act* means the Federal Food, Drug, and Cosmetic Act (secs. 201 *et seq.* (21 U.S.C. 321 *et seq.*)).

(2) *Active ingredient* means any component that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body of humans. The term includes those components that may undergo chemical change in the manufacture of the drug product and be present in the drug product in a modified form intended to furnish the specified activity or effect.

(3) *Approved drug application* means a new drug (NDA) or abbreviated new drug (ANDA) application approved under section 505 of the act (21 U.S.C. 355).

(4) *Bullet* means a geometric symbol that precedes each statement in a list of statements. For purposes of this section, the bullet style is limited to solid squares or solid circles, in the format set forth in paragraph (d)(4) of this section.

(5) *Established name* of a drug or ingredient thereof means the applicable official name designated under section 508 of the act (21 U.S.C. 358), or, if there is no designated official name and the drug or ingredient is recognized in an official compendium, the official title of the drug or ingredient in such compendium, or, if there is no designated official name and the drug

or ingredient is not recognized in an official compendium, the common or usual name of the drug or ingredient.

(6) *FDA* means the Food and Drug Administration.

(7) *Heading* means the required statements in quotation marks listed in paragraphs (c)(2) through (c)(9) of this section, excluding subheadings (as defined in paragraph (a)(9) of this section).

(8) *Inactive ingredient* means any component other than an active ingredient.

(9) *Subheading* means the required statements in quotation marks listed in paragraphs (c)(5)(ii) through (c)(5)(vii) of this section.

(10) *Drug facts labeling* means the title, headings, subheadings, and information required under or otherwise described in paragraph (c) of this section.

(11) *Title* means the heading listed at the top of the required OTC drug product labeling, as set forth in paragraph (c)(1) of this section.

(12) *Total surface area available to bear labeling* means all surfaces of the outside container of the retail package or, if there is no such outside container, all surfaces of the immediate container or container wrapper except for the flanges at the tops and bottoms of cans and the shoulders and necks of bottles and jars.

(c) *Content requirements.* The outside container or wrapper of the retail package, or the immediate container label if there is no outside container or wrapper, shall contain the title, headings, subheadings, and information set forth in paragraphs (c)(1) through (c)(8) of this section, and may contain the information under the heading in paragraph (c)(9) of this section, in the order listed.

(1) (Title) ''Drug Facts''. If the drug facts labeling appears on more than one panel, the title ''Drug Facts (continued)'' shall appear at the top of each subsequent panel containing such information.

(2) ''Active ingredient'' or ''Active ingredients'' ''(in each [insert the dosage unit stated in the directions for use (e.g., tablet, 5-mL teaspoonful) or in each gram as stated in §§ 333.110 and 333.120 of this chapter])'', followed by the established name of each active ingredient and

the quantity of each active ingredient per dosage unit. Unless otherwise provided in an applicable OTC drug monograph or approved drug application, products marketed without discrete dosage units (e.g., topicals) shall state the proportion (rather than the quantity) of each active ingredient.

(3) ''Purpose'' or ''Purposes'', followed by the general pharmacological category(ies) or the principal intended action(s) of the drug or, where the drug consists of more than one ingredient, the general pharmacological categories or the principal intended actions of each active ingredient. When an OTC drug monograph contains a statement of identity, the pharmacological action described in the statement of identity shall also be stated as the purpose of the active ingredient.

(4) ''Use'' or ''Uses'', followed by the indication(s) for the specific drug product.

(5) ''Warning'' or ''Warnings'', followed by one or more of the following, if applicable:

(i) ''For external use only'' [in bold type] for topical drug products not intended for ingestion, or ''For'' (select one of the following, as appropriate: ''rectal'' or ''vaginal'') ''use only'' [in bold type].

(ii) All applicable warnings listed in paragraphs (c)(5)(ii)(A) through (c)(5)(ii)(G) of this section with the appropriate subheadings highlighted in bold type:

(A) Allergic reaction warnings set forth in any applicable OTC drug monograph or approved drug application for any product that requires a separate allergy warning. This warning shall follow the subheading ''Allergy alert:''

(B) Reye's syndrome warning for drug products containing salicylates set forth in § 201.314(h)(1). This warning shall follow the subheading ''Reye's syndrome:''

(C) Flammability warning, with appropriate flammability signal word (e.g., §§ 358.150(c) and 358.550(c) of this chapter). This warning shall follow a subheading containing the appropriate flammability signal word described in an applicable OTC drug monograph or approved drug application.

(D) Water soluble gums warning set forth in § 201.319. This warning shall follow the subheading ''Choking:''

(E) Alcohol warning set forth in § 201.322. This warning shall follow the subheading ''Alcohol warning:''

(F) Sore throat warning set forth in § 201.315. This warning shall follow the subheading ''Sore throat warning:''

(G) Warning for drug products containing sodium phosphates set forth in § 201.307(b)(2)(i) or (b)(2)(ii). This warning shall follow the subheading ''Dosage warning:''

(iii) ''Do not use'' [in bold type], followed by all contraindications for use with the product. These contraindications are absolute and are intended for situations in which consumers should not use the product unless a prior diagnosis has been established by a doctor or for situations in which certain consumers should not use the product under any circumstances regardless of whether a doctor or health professional is consulted.

(iv) ''Ask a doctor before use if you have'' [in bold type] or, for products labeled only for use in children under 12 years of age, ''Ask a doctor before use if the child has'' [in bold type], followed by all warnings for persons with certain preexisting conditions (excluding pregnancy) and all warnings for persons experiencing certain symptoms. The warnings under this heading are those intended only for situations in which consumers should not use the product until a doctor is consulted.

(v) ''Ask a doctor or pharmacist before use if you are'' [in bold type] or, for products labeled only for use in children under 12 years of age, ''Ask a doctor or pharmacist before use if the child is'' [in bold type], followed by all drug-drug and drug-food interaction warnings.

(vi) ''When using this product'' [in bold type], followed by the side effects that the consumer may experience, and the substances (e.g., alcohol) or activities (e.g., operating machinery, driving a car, warnings set forth in § 369.21 of this chapter for drugs in dispensers pressurized by gaseous propellants) to avoid while using the product.

(vii) ''Stop use and ask a doctor if'' [in bold type], followed by any signs of toxicity or other reactions that would necessitate immediately discontinuing use of the product.

(viii) Any required warnings in an applicable OTC drug monograph, other OTC drug regulations, or approved drug application that do not fit within one of the categories listed in paragraphs (c)(5)(i) through (c)(5)(vii), (c)(5)(ix), and (c)(5)(x) of this section.

(ix) The pregnancy/breast-feeding warning set forth in § 201.63(a); the third trimester warning set forth in § 201.63(e) for products containing aspirin or carbaspirin calcium; the third trimester warning set forth in approved drug applications for products containing ketoprofen, naproxen sodium, and ibuprofen (not intended exclusively for use in children).

(x) The ''Keep out of reach of children'' warning and the accidental overdose/ingestion warning set forth in § 330.1(g) of this chapter.

(6) ''Directions'', followed by the directions for use described in an applicable OTC drug monograph or approved drug application.

(7) ''Other information'', followed by additional information that is not included under paragraphs (c)(2) through (c)(6), (c)(8), and (c)(9) of this section, but which is required by or is made optional under an applicable OTC drug monograph, other OTC drug regulation, or is included in the labeling of an approved drug application.

(i) Required information about certain ingredients in OTC drug products (e.g., sodium in § 201.64(c)) shall appear as follows: ''Each (insert appropriate dosage unit) contains.'' [in bold type] (insert name(s) of ingredient(s) and the quantity of each ingredient). This information shall be the first statement under this heading.

(ii) The phenylalanine/aspartame content required by § 201.21(b), if applicable, shall appear as the next item of information.

(iii) Additional information that is authorized to appear under this heading shall appear as the next item(s) of information. There is no required order for this subsequent information.

(8) ''Inactive ingredients'', followed by a listing of the established name of each inactive ingredient. If the product is an OTC drug product that is not also a cosmetic product, then the inactive ingredients shall be listed in alphabetical order. If the product is an OTC drug product that is also a cosmetic product, then the inactive ingredients shall be listed as set forth in § 701.3(a)

or (f) of this chapter, the names of cosmetic ingredients shall be determined in accordance with § 701.3(c) of this chapter, and the provisions in § 701.3(e), (g), (h)(l), (m), (n), and (o) of this chapter and § 720.8 of this chapter may also apply, as appropriate. If there is a difference in the labeling provisions in § 201.66 and §§ 701.3 and 720.8 of this chapter, the labeling provisions in § 201.66 shall be used.

(9) ''Questions?'' or ''Questions or comments?'', followed by the telephone number of a source to answer questions about the product. It is recommended that the days of the week and times of the day when a person is available to respond to questions also be included. ~~If a person is available to respond to questions 24 hours a day, 7 days a week, the day and time information may be~~ omitted. A graphic of a telephone or telephone receiver may appear before the heading. The telephone number must appear in a minimum 6-point bold type.

(d) *Format requirements.* The title, headings, subheadings, and information set forth in paragraphs (c)(1) through (c)(9) of this section shall be presented on OTC drug products in accordance with the following specifications. In the interest of uniformity of presentation, FDA strongly recommends that the Drug Facts labeling be presented using the graphic specifications set forth in appendix A to part 201.

(1) The title ''Drug Facts'' or ''Drug Facts (continued)'' shall use uppercase letters for the first letter of the words ''Drug'' and ''Facts.'' All headings and subheadings in paragraphs (c)(2) through (c)(9) of this section shall use an uppercase letter for the first letter in the first word and lowercase letters for all other words. The title, headings, and subheadings in paragraphs (c)(1), (c)(2), and (c)(4) through (c)(9) of this section shall be left justified.

(2) The letter height or type size for the title ''Drug Facts'' shall appear in a type size larger than the largest type size used in the Drug Facts labeling. The letter height or type size for the title ''Drug Facts (continued)'' shall be no smaller than 8-point type. The letter height or type size for the headings in paragraphs (c)(2) through (c)(9) of this section shall be the larger of either 8-point or greater type, or 2-point sizes greater than the point size of the text. The letter height

package, or the immediate container label if there is no outside container or wrapper. The continuation of the required content and format onto multiple panels must retain the required order and flow of headings, subheadings, and information. A visual graphic (e.g., an arrow) shall be used to signal the continuation of the Drug Facts labeling to the next adjacent panel.

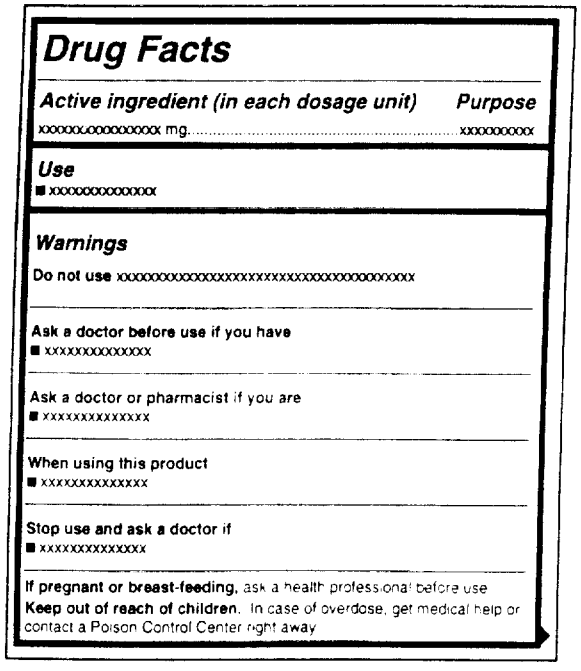
(6) The heading and information required under paragraph (c)(2) of this section shall appear immediately adjacent and to the left of the heading and information required under paragraph (c)(3) of this section. The active ingredients and purposes shall be aligned under the appropriate headings such that the heading and information required under paragraph (c)(2) of this section shall be left justified and the heading and information required under paragraph (c)(3) of this section shall be right justified. If the OTC drug product contains more than one active ingredient, the active ingredients shall be listed in alphabetical order. If more than one active ingredient has the same purpose, the purpose need not be repeated for each active ingredient, provided the information is presented in a manner that readily associates each active ingredient with its purpose (i.e., through the use of brackets, dot leaders, or other graphical features). The information described in paragraphs (c)(4) and (c)(6) through (c)(9) of this section may start on the same line as the required headings. None of the information described in paragraph (c)(5) of this section shall appear on the same line as the ''Warning'' or ''Warnings'' heading.

(7) Graphical images (e.g., the UPC symbol) and information not described in paragraphs (c)(1) through (c)(9) of this section shall not appear in or in any way interrupt the required title, headings, subheadings, and information in paragraphs (c)(1) through (c)(9) of this section. Hyphens shall not be used except to punctuate compound words.

(8) The information described in paragraphs (c)(1) through (c)(9) of this section shall be set off in a box or similar enclosure by the use of a barline. A distinctive horizontal barline extending to each end of the ''Drug Facts'' box or similar enclosure shall provide separation between each of the headings listed in paragraphs (c)(2) through (c)(9) of this section. When a reading listed in paragraphs (c)(2) through (c)(9) of this section appears on a subsequent panel immediately after

(iv) Paragraph (d)(8) of this section shall apply except that the box or similar enclosure required in paragraph (d)(8) may be omitted if the Drug Facts labeling is set off from the rest of the labeling by use of color contrast (i.e., type shall be all black or one dark color type, printed on a white or other light neutral color contrasting background).

(11)(i) The following labeling outlines the various provisions in paragraphs (c) and (d) of this section:



Drug Facts

Active ingredient (in each dosage unit) ***Purpose***

xxxxxx.xxxxxxxxxx mg xxxxxxxxx

Use

■ xxxxxxxxxxxxx

Warnings

Do not use xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx

Ask a doctor before use if you have

■ xxxxxxxxxxxxx

Ask a doctor or pharmacist if you are

■ xxxxxxxxxxxxx

When using this product

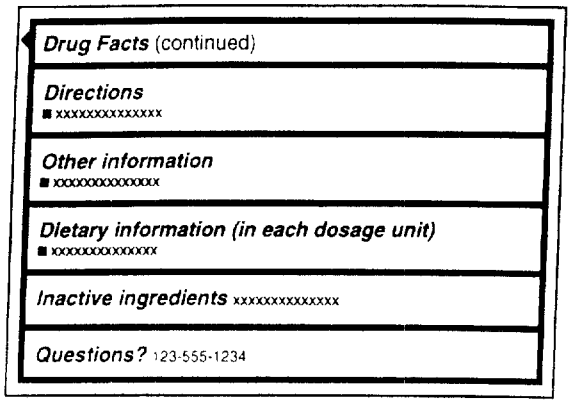
■ xxxxxxxxxxxxx

Stop use and ask a doctor if

■ xxxxxxxxxxxxx

If pregnant or breast-feeding, ask a health professional before use.

Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.



Drug Facts (continued)

Directions

■ xxxxxxxxxxxxx

Other information

■ xxxxxxxxxxxxx

Dietary information (in each dosage unit)

■ xxxxxxxxxxxxx

Inactive ingredients xxxxxxxxxxxxx

Questions? 123-555-1234

(ii) The following sample label illustrates the provisions in paragraphs (c) and (d) of this section:

L088

Drug Facts

Active ingredient (in each tablet) — **Purpose**

Chlorpheniramine maleate 4 mg ..... Antihistamine

Uses temporarily relieves these symptoms due to hay fever or other upper respiratory allergies: ■ sneezing ■ runny nose ■ itchy, watery eyes ■ itchy throat

Warnings

Ask a doctor before use if you have

■ glaucoma ■ a breathing problem such as emphysema or chronic bronchitis
■ trouble urinating due to an enlarged prostate gland

Ask a doctor or pharmacist before use if you are taking tranquilizers or sedatives

When using this product

■ marked drowsiness may occur ■ avoid alcoholic drinks
■ alcohol, tranquilizers, and sedatives may increase drowsiness
■ be careful when driving a motor vehicle or operating machinery
■ excitability may occur, especially in children

If pregnant or breast-feeding, ask a health professional before use.

Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.

Directions

adults and children 12 years and over	take 2 tablets every 8 hours as needed not more than 6 tablets in 24 hours
children 6 years to under 12 years	take 1 tablet every 8 hours as needed not more than 3 tablets in 24 hours
children under 6 years	ask a doctor

Drug Facts (continued)

Other information ■ store at 20-25°C (68-77°F) ■ protect from excessive moisture

Inactive ingredients D&C yellow no. 10, lactose, magnesium stearate, microcrystalline cellulose, pregelatinized starch

(iii) The following sample label illustrates the provisions in paragraphs (c) and (d) of this section, including paragraph (d)(10), which permits modifications for small packages:

Drug Facts

Active ingredients (in each tablet)	Purpose
Aluminum hydroxide gel 200 mg	Antacid
Magnesium hydroxide 200 mg	Antacid
Simethicone 25 mg	Antigas

Uses

- relieves symptoms referred to as gas
- relieves ■ heartburn ■ acid indigestion ■ sour stomach ■ upset stomach due to these symptoms

Warnings

Ask a doctor before use if you have kidney disease

Ask a doctor or pharmacist before use if you are taking a prescription drug. Antacids may interact with certain prescription drugs

Stop use and ask a doctor if symptoms last more than 2 weeks

Keep out of reach of children.

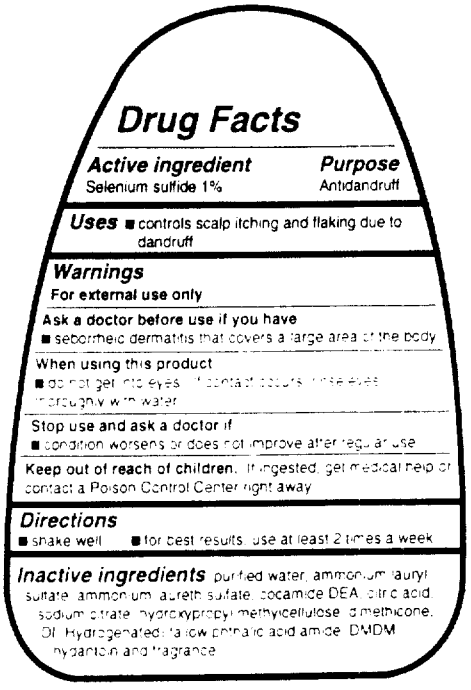
Directions

- chew 1 to 4 tablets 4 times daily
- do not take more than 16 tablets in 24 hours or use the maximum dosage for more than 2 weeks

Inactive ingredients D&C red no. 30, D&C yellow no. 10, dextrose, FD&C blue no. 1, glycerin, magnesium stearate, mannitol, sodium saccharin, sodium starch, starch, sugar, talc

(iv) The following sample label illustrates the provisions in paragraphs (c) and (d) of this section for a drug product marketed with cosmetic claims:

140a



Drug Facts

Active ingredient Selenium sulfide 1%

Purpose Antidandruff

Uses ■ controls scalp itching and flaking due to dandruff

Warnings

For external use only

Ask a doctor before use if you have
■ seborrheic dermatitis that covers a large area of the body

When using this product
■ do not get into eyes ■ if contact occurs, rinse eyes thoroughly with water

Stop use and ask a doctor if
■ condition worsens or does not improve after regular use

Keep out of reach of children. If ingested, get medical help or contact a Poison Control Center right away

Directions
■ shake well ■ for best results, use at least 2 times a week

Inactive ingredients purified water, ammonium lauryl sulfate, ammonium laureth sulfate, cocamide DEA, citric acid, sodium citrate, hydroxypropyl methylcellulose, dimethicone, DI Hydrogenated Tallow phthalic acid amide, DMDM hydantoin and fragrance

(e) *Exemptions and deferrals.* FDA on its own initiative or in response to a written request from any manufacturer, packer, or distributor, may exempt or defer, based on the circumstances presented, one or more specific requirements set forth in this section on the basis that the requirement is inapplicable, impracticable, or contrary to public health or safety. Requests for exemptions shall be submitted in three copies in the form of an ''Application for Exemption'' to the Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. The request shall be clearly identified on the envelope as a ''Request for Exemption from 21 CFR 201.66 (OTC Labeling Format)'' and shall be directed to Docket No. 98N–0337. A separate request shall be submitted for each OTC drug product. Sponsors of a product marketed under an approved drug application shall also submit a single copy of the exemption request to their application. Decisions on exemptions and deferrals shall be maintained in a permanent file in this docket for public review. Exemption and deferral requests shall:

(i) Document why a particular requirement is inapplicable, impracticable, or contrary to public health or safety; and

(ii) Include a representation of the proposed labeling, including any outserts, panel extensions, or other graphical or packaging techniques intended to be used with the product.

(f) *Interchangeable terms and connecting terms.* The terms listed in § 330.1(i) of this chapter may be used interchangeably in the labeling of OTC drug products, provided such use does not alter the meaning of the labeling that has been established and identified in an applicable OTC drug monograph or by regulation. The terms listed in § 330.1(j) of this chapter may be deleted from the labeling of OTC drug products when the labeling is revised to comply with this section, provided such deletion does not alter the meaning of the labeling that has been established and identified in an applicable OTC drug monograph or by regulation. The terms listed in § 330.1(i) and (j) of this chapter shall not be used to change in any way the specific title, headings, and subheadings required under paragraphs (c)(1) through (c)(9) of this section.

(g) *Regulatory action.* An OTC drug product that is not in compliance with the format and content requirements in this section is subject to regulatory action.

5. Section 201.314 is amended by revising the first two sentences in paragraph (a) and by revising paragraphs (g)(1) and (h)(1) to read as follows:

§ 201.314 Labeling of drug preparations containing salicylates.

(a) The label of any oral drug preparation intended for sale without prescription and which contains any salicylate ingredient (including aspirin, salicylamide, other salicylates, and combinations) must conspicuously bear, on a clearly contrasting background, the warning statement: ''Keep out of reach of children [highlighted in bold type]. In case of overdose, get medical help or contact a Poison Control Center right away,'' or ''Keep out of reach of children [highlighted in bold type],'' except that if the article is an aspirin preparation, it shall bear the first of these warning statements. * * *

* * * * *

(g)(1) The label of any drug containing more than 5 percent methyl salicylate (wintergreen oil) should bear a conspicuous warning such as: ''Do not use otherwise than as directed.'' These drug products must also include the ''Keep out of reach of children'' warning and the accidental ingestion warning as required in § 330.1(g) of this chapter.

* * * * *

(h)(1) The labeling of orally or rectally administered over-the-counter aspirin and aspirin-containing drug products subject to this paragraph is required to prominently bear a warning. The warning shall be as follows: ''Children and teenagers should not use this medicine for chicken pox or flu symptoms before a doctor is consulted about Reye syndrome, a rare but serious illness reported to be associated with aspirin.''

* * * * *

6. Section 201.319 is amended by revising paragraph (b) to read as follows:

§ 201.319 Water-soluble gums, hydrophilic gums, and hydrophilic mucilloids (including, but not limited to agar, alginic acid, calcium polycarbophil, carboxymethylcellulose sodium, carrageenan, chondrus, glucomannan ((B-1,4, linked) polymannose acetate), guar gum, karaya gum, kelp, methylcellulose, plantago seed (psyllium), polycarbophil, tragacanth, and xanthan gum) as active ingredients; required warnings and directions.

* * * * *

(b) Any drug products for human use containing a water-soluble gum, hydrophilic gum, or hydrophilic mucilloid as an active ingredient in an oral dosage form when marketed in a dry or incompletely hydrated form as described in paragraph (a) of this section are misbranded within the meaning of section 502 of the Federal Food, Drug, and Cosmetic Act unless their labeling bears the following warnings (under the subheading ''Choking'') and directions:

'''Choking' [highlighted in bold type]: Taking this product without adequate fluid may cause it to swell and block your throat or esophagus and may cause choking. Do not take this product if you have difficulty in swallowing. If you experience chest pain, vomiting, or difficulty in swallowing or breathing after taking this product, seek immediate medical attention;'' and

'''Directions' [highlighted in bold type]:'' (Select one of the following, as appropriate: ''Take'' or ''Mix'') ''this product (child or adult dose) with at least 8 ounces (a full glass) of water or other fluid. Taking this product without enough liquid may cause choking. See choking warning.''

* * * * *

7. Appendix A is added to part 201 to read as follows:

Appendix A to Part 201—Graphic Enhancements

I. Section 201.66 Standard Labeling Format

A. Overall

1. The "Drug Facts" information is set off in a box or similar enclosure by the use of a barline with all black or one dark color type printed on a white or other light, neutral color, contrasting background.

B. Typeface and size

1. The "Drug Facts" labeling uses 6 point or larger Helvetica Bold, Helvetica Bold Italic, and/or Helvetica Regular type.

2. "Drug Facts" is set in 14 point Helvetica Bold Italic, left justified.

3. "Drug Facts (continued)" is set in 8 point Helvetica Bold Italic for the words "Drug Facts" and 8 point Helvetica Regular for the word "(continued)" and is left justified.

4. The headings (e.g., "Directions") are set in 8 point Helvetica Bold Italic, left justified.

5. The subheadings (e.g., "Ask a doctor or pharmacist before use if you are") are set in 6 point Helvetica Bold, left justified.

6. The body text is set in 6 point Helvetica Regular with 6.5 point leading, left justified.

7. The heading "Purpose" is right justified.

8. The bullet is a 5 point solid square.

9. Two em spacing separates bullets when more than one bullet is on the same line.

10. A table format is used for 3 or more dosage directions.

11. A graphic appears at the bottom of the first panel leading the reader to the next panel.

C. Barlines and hairlines

1. A 2.5-point horizontal barline extends to each end of the "Drug Facts" box (or similar enclosure), providing separation between each of the headings.

2. A 0.5-point horizontal hairline extends within 2 spaces on either side of the ''Drug Facts'' box (or similar enclosure), immediately following the title and immediately preceding the subheadings.

3. A 0.5-point horizontal hairline follows the title, immediately preceding the heading, when a heading appears on a subsequent panel immediately after the ''Drug Facts (continued)'' title.

D. Box or Enclosure

1. All information is enclosed by a 2.5-point barline.

II. Section 201.66 Modified Labeling Format

A. Overall

1. The ''Drug Facts'' information is presented by color contrast (all black or one dark color type printed on a white or other light, neutral color, contrasting background). The box barline is omitted.

B. Typeface and size

1. The ''Drug Facts'' labeling uses 6 point or larger Helvetica Bold, Helvetica Bold Italic, and/or Helvetica Regular type.

2. ''Drug Facts'' is set in 9 point Helvetica Bold Italic, left justified.

3. The headings (e.g., ''Directions'') are set in 8 point Helvetica Bold Italic, left justified.

4. The subheadings (e.g., ''Ask a doctor or pharmacist before use if you are'') are set in 6 point Helvetica Bold, left justified.

5. The body text is set in 6 point Helvetica Regular with 6.5 point leading, left justified.

6. The heading ''Purpose'' is right justified.

7. The bullet is a 5 point solid square.

8. Bulleted information may start on same line as headings (except for the ''Warnings'' heading) and subheadings, with 2 em spacing separating bullets, and need not be vertically aligned.

C. Barlines and hairlines

1. A 2.5-point horizontal barline extends to each end of the ''Drug Facts'' box (or similar enclosure), providing separation between each of the headings.

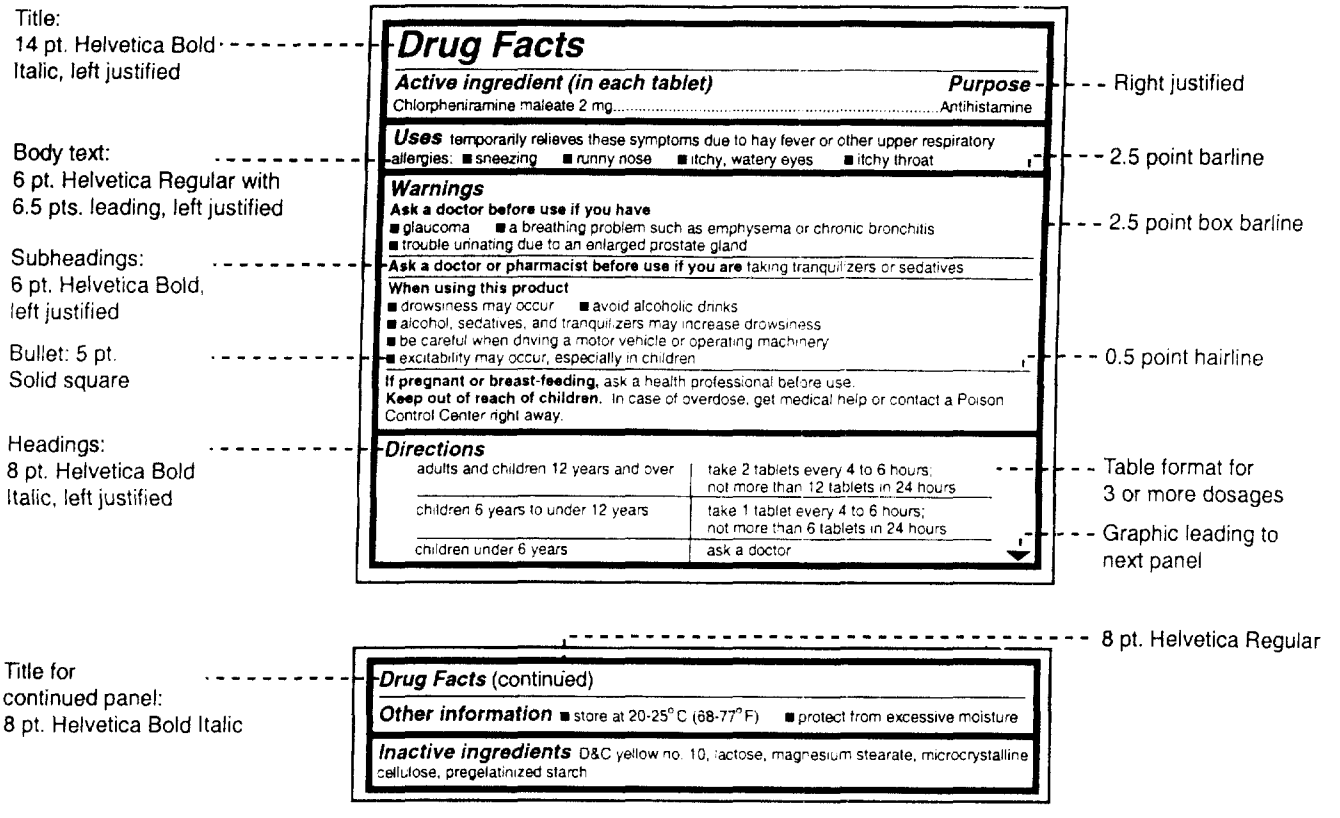
2. A 0.5-point horizontal hairline extends within 2 spaces on either side of the ''Drug Facts'' box (or similar enclosure), immediately following the title and immediately preceding the subheadings.

D. Box or Enclosure

1. All information is set off by color contrast (dark type on light background). No barline used.

Appendix A to Part 201

I. Section 201.66 Standard Labeling Format


Title:
14 pt. Helvetica Bold Italic, left justified
Body text:
6 pt. Helvetica Regular with 6.5 pts. leading, left justified
Subheadings:
6 pt. Helvetica Bold, left justified
Bullet: 5 pt. Solid square
Headings:
8 pt. Helvetica Bold Italic, left justified
Drug Facts
Active ingredient (in each tablet)
Purpose
Chlorpheniramine maleate 2 mg
Antihistamine
Uses temporarily relieves these symptoms due to hay fever or other upper respiratory allergies: ■ sneezing ■ runny nose ■ itchy, watery eyes ■ itchy throat
Warnings
Ask a doctor before use if you have
■ glaucoma ■ a breathing problem such as emphysema or chronic bronchitis
■ trouble urinating due to an enlarged prostate gland
Ask a doctor or pharmacist before use if you are taking tranquilizers or sedatives
When using this product
■ drowsiness may occur ■ avoid alcoholic drinks
■ alcohol, sedatives, and tranquilizers may increase drowsiness
■ be careful when driving a motor vehicle or operating machinery
■ excitability may occur, especially in children
If pregnant or breast-feeding, ask a health professional before use.
Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.
Directions
adults and children 12 years and over | take 2 tablets every 4 to 6 hours; not more than 12 tablets in 24 hours
children 6 years to under 12 years | take 1 tablet every 4 to 6 hours; not more than 6 tablets in 24 hours
children under 6 years | ask a doctor
Right justified
2.5 point barline
2.5 point box barline
0.5 point hairline
Table format for 3 or more dosages
Graphic leading to next panel
8 pt. Helvetica Regular
Title for continued panel:
8 pt. Helvetica Bold Italic
Drug Facts (continued)
Other information ■ store at 20-25°C (68-77°F) ■ protect from excessive moisture
Inactive ingredients D&C yellow no. 10, lactose, magnesium stearate, microcrystalline cellulose, pregelatinized starch

II. Section 201.66 Modified Labeling Format

PART 330—OVER-THE-COUNTER (OTC) HUMAN DRUGS WHICH ARE GENERALLY RECOGNIZED AS SAFE AND EFFECTIVE AND NOT MISBRANDED

8. The authority citation for 21 CFR part 330 continues to read as follows:

Authority: 21 U.S.C. 321, 351, 352, 353, 355, 360, 371.

9. Section 330.1 is amended by revising paragraphs (c)(1), (c)(2), (i), and (j), and by removing the first three sentences in paragraph (g) and adding two sentences in their place to read as follows:

§ 330.1 General conditions for general recognition as safe, effective, and not misbranded.

* * * * *

(c)(1) The product is labeled in compliance with chapter V of the Federal Food, Drug, and Cosmetic Act (the act) and subchapter C *et seq.* of this chapter, including the format and content requirements in § 201.66 of this chapter. An OTC drug product that is not in compliance with chapter V and subchapter C, including § 201.66, is subject to regulatory action. For purposes of § 201.61(b) of this chapter, the statement of identity of the product shall be the term or phrase used in the applicable OTC drug monograph established in this part.

(2) The ''Uses'' section of the label and labeling of the product shall contain the labeling describing the ''Indications'' that have been established in an applicable OTC drug monograph or alternative truthful and nonmisleading statements describing only those indications for use that have been established in an applicable monograph, subject to the provisions of section 502 of the act relating to misbranding and the prohibition in section 301(d) of the act against the introduction or delivery for introduction into interstate commerce of unapproved new drugs in violation of section 505(a) of the act. Any other labeling under this subchapter and subchapter C *et seq.* of this chapter shall be stated in the exact language where exact language has been

established and identified by quotation marks in an applicable OTC drug monograph or by regulation (e.g., § 201.63 of this chapter), except as provided in paragraphs (i) and (j) of this section.

* * * * *

(g) The labeling for all drugs contains the general warning: ''Keep out of reach of children.'' [highlighted in bold type]. The labeling of drugs shall also state as follows: For drugs used by oral administration, ''In case of overdose, get medical help or contact a Poison Control Center right away''; for drugs used topically, rectally, or vaginally and not intended for oral ingestion, ''If swallowed, get medical help or contact a Poison Control Center right away''; and for drugs used topically and intended for oral use, ''If more than used for'' (insert intended use, e.g., pain) ''is accidentally swallowed, get medical help or contact a Poison Control Center right away.''

* * *

* * * * *

(i) The following terms may be used interchangeably in the labeling of OTC drug products, provided such use does not alter the meaning of the labeling that has been established and identified in an applicable monograph or by regulation. The following terms shall not be used to change in any way the title, headings, and subheadings required under § 201.66(c)(1) through (c)(9) of this chapter:

(1) ''Abdominal'' or ''stomach'' (in context only).

(2) ''Administer'' or ''give''.

(3) ''Aggravate(s)'' or ''make(s) worse''.

(4) ''Application of this product'' or ''applying''.

(5) ''Are uncertain'' or ''do not know''.

(6) ''Ask'' or ''consult'' or ''contact''.

(7) ''Asking'' or ''consulting''.

(8) ''Assistance'' or ''help'' or ''aid''.

(9) ''Associated with'' or ''due to'' or ''caused by''.

(10) ''Avoid contact with eyes'' or ''do not get into eyes''.

(11) ''Avoid inhaling'' or ''do not inhale''.

(12) ''Before a doctor is consulted'' or ''without first consulting your doctor'' or ''consult your doctor before''.

(13) ''Beverages'' or ''drinks''.

(14) ''Clean'' or ''cleanse''.

(15) ''Consulting'' or ''advising''.

(16) ''Continue(s)'' or ''persist(s)'' or ''is persistent'' or ''do(es) not go away'' or ''last(s)''.

(17) ''Daily'' or ''every day''.

(18) ''Develop(s)'' or ''begin(s)'' or ''occur(s)''.

(19) ''Difficulty'' or ''trouble''.

(20) ''Difficulty in urination'' or ''trouble urinating''.

(21) ''Discard'' or ''throw away''.

(22) ''Discontinue'' or ''stop'' or ''quit''.

(23) ''Doctor'' or ''physician''.

(24) ''Drowsiness'' or ''the drowsiness effect''. add (25) "Drowsiness may occur" or "you may get drowsy".

(26) ''Enlargement of the'' or ''an enlarged''.

(27) ''Exceed'' or ''use more than'' or ''go beyond''. add (27) "especially in children" or "especially children".

(28) ''Exceed recommended dosage'' or ''use more than directed''.

(29) ''Excessive'' or ''too much''.

(30) ''Experience'' or ''feel''. add (31) "Excitability may occur" or "you may get excited".

(31) ''For relief of'' or ''relieves''.

(32) ''For temporary reduction of'' or ''temporarily reduces''.

(33) ''For the temporary relief of'' or ''temporarily relieves''.

(34) ''For the treatment of'' or ''treats''.

(35) ''Frequently'' or ''often''.

(36) ''Give to'' or ''use in''.

(36) ''Immediately'' or ''right away'' or ''directly''.

(37) ''Immediately'' or ''as soon as''.

(38) ''Immediately following'' or ''right after''.

(39) ''Improve(s)'' or ''get(s) better'' or ''make(s) better''.

(40) ''Increased'' or ''more''.

(41) ''Increase your risk of'' or ''cause''.

(42) ''Indication(s)'' or ''Use(s)''.

(43) ''Inhalation'' or ''puff''.

(44) ''In persons who'' or ''if you'' or ''if the child''.

(45) ''Instill'' or ''put''.

(46) ''Is (are) accompanied by'' or ''you also have'' (in context only) or ''(optional: that) occur(s) with''.

(47) ''Longer'' or ''more''.

(48) ''Lung'' or ''pulmonary''.

(49) ''Medication(s)'' or ''medicine(s)'' or ''drug(s)''.

(50) ''Nervousness, dizziness, or sleeplessness occurs'' or ''you get nervous, dizzy, or sleepless''.

(51) ''Not to exceed'' or ''do not exceed'' or ''not more than''.

(52) ''Obtain(s)'' or ''get(s)''.

(53) ''Passages'' or ''passageways'' or ''tubes''.

(54) ''Perforation of'' or ''hole in''.

(55) ''Persistent'' or ''that does not go away'' or ''that continues'' or ''that lasts''.

(56) ''Per day'' or ''daily''.

(57) ''Presently'' or ''now''.

(58) ''Produce(s)'' or ''cause(s)''.

(59) ''Prompt(ly)'' or ''quick(ly)'' or ''right away''.

(60) ''Reduce'' or ''minimize''.

(61) ''Referred to as'' or ''of''.

(62) ''Sensation'' or ''feeling''.

(63) ''Solution'' or ''liquid''.

(64) ''Specifically'' or ''definitely''.

(65) ''Take'' or ''use'' or ''give''.

(66) ''Tend(s) to recur'' or ''reoccur(s)'' or ''return(s)'' or ''come(s) back''.

(67) ''To avoid contamination'' or ''avoid contamination'' or ''do not contaminate''.

(68) ''To help'' or ''helps''.

(69) ''Unless directed by a doctor'' or ''except under the advice of a doctor'' or ''unless told to do so by a doctor''.

(70) ''Use caution'' or ''be careful''.

(71) ''Usually'' or ''generally'' (in context only).

(72) ''You'' (''Your'') or ''the child'' (''the child's'').

(73) ''You also have'' or ''occurs with''.

(74) ''When practical'' or ''if possible''.

(75) ''Whether'' or ''if''.

(76) ''Worsen(s)'' or ''get(s) worse'' or ''make(s) worse''.

(j) The following connecting terms may be deleted from the labeling of OTC drug products, provided such deletion does not alter the meaning of the labeling that has been established and identified in an applicable monograph or by regulation. The following terms shall not be used to change in any way the specific title, headings, and subheadings required under § 201.66(c)(1) through (c)(9) of this chapter:

(1) ''And''.

(2) ''As may occur with''.

(3) ''Associated'' or ''to be associated''.

(4) ''Consult a doctor''.

(5) ''Discontinue use''.

(d) *Drug interaction precaution.* The labeling of the product contains the following statement ''Ask a doctor or pharmacist before use if you are [bullet][1] presently taking a prescription drug. Antacids may interact with certain prescription drugs.''

* * * * *

PART 341—COLD, COUGH, ALLERGY, BRONCHODILATOR, AND ANTIASTHMATIC DRUG PRODUCTS FOR OVER–THE–COUNTER HUMAN USE

12. The authority citation for 21 CFR part 341 continues to read as follows:

Authority: 21 U.S.C. 321, 351, 352, 353, 355, 360, 371.

13. Section 341.74 is amended by revising paragraphs (c)(4)(v) and (c)(4)(vi) to read as follows:

§ 341.74 Labeling of antitussive drug products.

* * * * *

(c) * * *

(4) * * *

(v) *For products containing dextromethorphan or dextromethorphan hydrobromide as identified in § 341.14(a)(3) and (a)(4) when labeled for adults or for adults and children under 12 years of age. Drug interaction precaution.* ''Do not use if you are now taking a prescription monoamine oxidase inhibitor (MAOI) (certain drugs for depression, psychiatric, or emotional conditions, or Parkinson's disease), or for 2 weeks after stopping the MAOI drug. If you do not know if your prescription drug contains an MAOI, ask a doctor or pharmacist before taking this product.''

(vi) *For products containing dextromethorphan or dextromethorphan hydrobromide as identified in § 341.14(a)(3) and (a)(4) when labeled only for children under 12 years of age. Drug*

[1] See § 201.66(b)(4) of this chapter.

interaction precaution. ''Do not give to a child who is taking a prescription monoamine oxidase inhibitor MAOI) (certain drugs for depression, psychiatric, or emotional conditions, or Parkinson's disease), or for 2 weeks after stopping the MAOI drug. If you do not know if your child's prescription drug contains an MAOI, ask a doctor or pharmacist before giving this product.''

* * * * *

14. Section 341.76 is amended by revising paragraph (c)(4) to read as follows:

§ 341.76 Labeling of bronchodilator drug products.

* * * * *

(c) * * *

(4) *Drug interaction precaution.* ''Do not use ~~this product~~ if you are now taking a prescription monoamine oxidase inhibitor (MAOI) (certain drugs for depression, psychiatric, or emotional conditions, or Parkinson's disease), or for 2 weeks after stopping the MAOI drug. If you do not know if your prescription drug contains an MAOI, ask a doctor or pharmacist before taking this product.''

* * * * *

15. Section 341.80 is amended by revising paragraphs (c)(1)(i)(D) and (c)(1)(ii)(D) to read as follows:

§ 341.80 Labeling of nasal decongestant drug products.

* * * * *

(c) * * *

(1) * * *

(i) * * *

(D) *Drug interaction precaution.* ''Do not use if you are now taking a prescription monoamine oxidase inhibitor (MAOI) (certain drugs for depression, psychiatric, or emotional conditions, or

Parkinson's disease), or for 2 weeks after stopping the MAOI drug. If you do not know if your prescription drug contains an MAOI, ask a doctor or pharmacist before taking this product.''

(ii) * * *

(D) *Drug interaction precaution.* ''Do not give to a child who is taking a prescription monoamine oxidase inhibitor (MAOI) (certain drugs for depression, psychiatric, or emotional conditions, or Parkinson's disease), or for 2 weeks after stopping the MAOI drug. If you do not know if your child's prescription drug contains an MAOI, ask a doctor or pharmacist before giving this product.''

* * * * *

PART 346—ANORECTAL DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE

16. The authority citation for 21 CFR part 346 continues to read as follows:

Authority: 21 U.S.C. 321, 351, 352, 353, 355, 360, 371.

17. Section 346.50 is amended by revising paragraph (c)(7)(ii) to read as follows:

§ 346.50 Labeling of anorectal drug products.

* * * * *

(c) * * *

(7) * * *

(ii) ''Ask a doctor or pharmacist before use if you are [bullet][1] presently taking a prescription drug for high blood pressure or depression.''

* * * * *

[1] See § 201.66(b)(4) of this chapter.

PART 355—ANTICARIES DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE

18. The authority citation for 21 CFR part 355 continues to read as follows:

Authority: 21 U.S.C. 321, 351, 352, 353, 355, 360, 371.

19. Section 355.50 is amended by revising paragraphs (c)(1) and (c)(2) to read as follows:

§ 355.50 Labeling of anticaries drug products.

* * * * *

(c) * * *

(1) *For all fluoride dentifrice (gel, paste, and powder) products.* ''Keep out of reach of children under 6 years of age. [highlighted in bold type] If more than used for brushing is accidentally swallowed, get medical help or contact a Poison Control Center right away.'' These warnings shall be used in place of the general warning statements required by § 330.1(g) of this chapter.

(2) *For all fluoride rinse and preventive treatment gel products.* ''Keep out of reach of children. [highlighted in bold type] If more than used for'' (select appropriate word: ''brushing'' or ''rinsing'') ''is accidentally swallowed, get medical help or contact a Poison Control Center right away.'' These warnings shall be used in place of the general warning statements required by § 330.1(g) of this chapter.

* * * * *

PART 358—MISCELLANEOUS EXTERNAL DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE

20. The authority citation for 21 CFR part 358 continues to read as follows:

Authority: 21 U.S.C. 321, 351, 352, 353, 355, 360, 371.

21. Section 358.650 is amended in paragraph (d)(1) by revising the information in the brackets to read as follows:

§ 358.650 Labeling of pediculicide drug products.

* * * * *

(d) * * *

(1) * * * [sentence in boldface type].

* * * * *

PART 369—INTERPRETATIVE STATEMENTS RE WARNINGS ON DRUGS AND DEVICES FOR OVER–THE–COUNTER SALE

22. The authority citation for 21 CFR part 369 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 371.

23. Section 369.9 is revised to read as follows:

§ 369.9 General warnings re accidental ingestion by children.

Section 369.20 includes under certain items, but not all medicines, the statement: ''Keep this and all medicines out of children's reach. In case of overdose, get medical help or contact a Poison Control Center right away,'' or ''Keep out of reach of children.'' However, in view of the possibility of accidental ingestion of drugs, it is not only suggested but is recommended that one of these statements be used on the label of all drug products.

§ 369.20 Drugs; recommended warning and caution statements.

24. The entry ''NUX VOMICA AND STRYCHNINE PREPARATIONS.'' is revised to read as follows:

NUX VOMICA AND STRYCHNINE PREPARATIONS.

"Do not use more than the recommended dosage. Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away."

25. The entry "SALICYLATES, INCLUDING ASPIRIN * * *." is revised to read as follows:

SALICYLATES, INCLUDING ASPIRIN AND SALICYLAMIDE (EXCEPT METHYL SALICYLATE, EFFERVESCENT SALICYLATE PREPARATIONS, AND PREPARATIONS OF AMINOSALICYLIC ACID AND ITS SALTS). (See also § 201.314 of this chapter.)

"Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away;" or "Keep out of reach of children."

If the article is an aspirin preparation, it should bear the first of the above two warning statements. In either case, the above information should appear on the label.

Caution—For children under 3 years of age, consult your physician; or

Caution—For younger children, consult your physician.

One of the two immediately preceding caution statements is required on the label of all aspirin tablets, but such a statement is not required on the labels of other salicylates clearly offered for administration to adults only.

If offered for use in arthritis or rheumatism, in juxtaposition therewith, the statement:

Caution—If pain persists for more than 10 days, or redness is present, or in conditions affecting children under 12 years of age, consult a physician immediately.

26. The entry "SALICYLATES: METHYL SALICYLATE (WINTERGREEN OIL)." is revised to read as follows:

SALICYLATES: METHYL SALICYLATE (WINTERGREEN OIL). (See also §§ 201.303 and 201.314 of this chapter.)

"Do not use otherwise than as directed. Keep out of reach of children to avoid accidental poisoning. If swallowed, get medical help or contact a Poison Control Center right away."

If the preparation is a counter-irritant or rubefacient the statement:

Caution—Discontinue use if excessive irritation of the skin develops. Avoid getting into the eyes or on mucous membranes.

If offered for use in arthritis or rheumatism, in juxtaposition therewith, the statement:

Caution—If pain persists for more than 10 days, or redness is present, or in conditions affecting children under 12 years of age consult a physician immediately.

27. The entry "ZINC STEARATE DUSTING POWDERS." is revised to read as follows:

ZINC STEARATE DUSTING POWDERS.

"Keep out of reach of children; avoid inhaling. If swallowed, get medical help or contact a Poison Control Center right away."

§ 369.21 Drugs; warning and caution statements required by regulations.

28. The entry "'COUGH–DUE–TO–COLD' PREPARATIONS (CARBETAPENTANE CITRATE)." is revised to read as follows:

"COUGH–DUE–TO–COLD" PREPARATIONS (CARBETAPENTANE CITRATE). (See § 310.201(a)(20) of this chapter.)

"Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away."

29. The entry "SODIUM GENTISATE." is revised to read as follows:

SODIUM GENTISATE. (See §§ 201.314 and 310.301(a)(2) of this chapter.)

Warning—Do not give to children under 6 years of age or use for prolonged period unless directed by physician.

"Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away."

If offered for use in arthritis or rheumatism, in juxtaposition therewith, the statement:

Caution—If pain persists for more than 10 days, or redness is present, or in conditions affecting children under 12 years of age, consult a physician immediately.

PART 701—COSMETIC LABELING

30. The authority citation for 21 CFR part 701 continues to read as follows:

Authority: 21 U.S.C. 321, 352, 361, 362, 363, 371, 374; 15 U.S.C. 1454, 1455.

31. Section 701.3 is amended by revising paragraph (d) to read as follows:

§ 701.3 Designation of ingredients.

* * * * *

(d) Where a cosmetic product is also an over-the-counter drug product, the declaration shall declare the active drug ingredients as set forth in § 201.66(c)(2) and (d) of this chapter, and the

declaration shall declare the cosmetic ingredients as set forth in § 201.66(c)(8) and (d) of this chapter.

* * * * *

Dated: _____

Jane E. Henney,

Commissioner for Food and Drugs.

Donna E. Shalala,

Secretary of Health and Human Services.

[FR Doc. 99–???? Filed ??–??–99; 8:45 am]

BILLING CODE 4160–01–F

[The following Appendix A will not appear in the Code of Federal Regulations.]

Appendix A.- Examples of Prototype OTC Drug Product Labeling

Example 1

Single Ingredient Product Using Standard Labeling Format*

Drug Facts

Active ingredient (in each tablet)	Purpose
Chlorpheniramine maleate 2 mg	Antihistamine

Uses temporarily relieves these symptoms due to hay fever or other upper respiratory allergies: ■ sneezing ■ runny nose ■ itchy, watery eyes ■ itchy throat

Warnings

Ask a doctor before use if you have
■ glaucoma ■ a breathing problem such as emphysema or chronic bronchitis
■ trouble urinating due to an enlarged prostate gland

Ask a doctor or pharmacist before use if you are taking tranquilizers or sedatives

When using this product
■ drowsiness may occur ■ avoid alcoholic drinks
■ alcohol, sedatives, and tranquilizers may increase drowsiness
■ be careful when driving a motor vehicle or operating machinery
■ excitability may occur, especially in children

If **pregnant or breast-feeding,** ask a health professional before use.
Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.

Directions

adults and children 12 years and over	take 2 tablets every 4 to 6 hours; not more than 12 tablets in 24 hours
children 6 years to under 12 years	take 1 tablet every 4 to 6 hours; not more than 6 tablets in 24 hours
children under 6 years	ask a doctor

Drug Facts (continued)

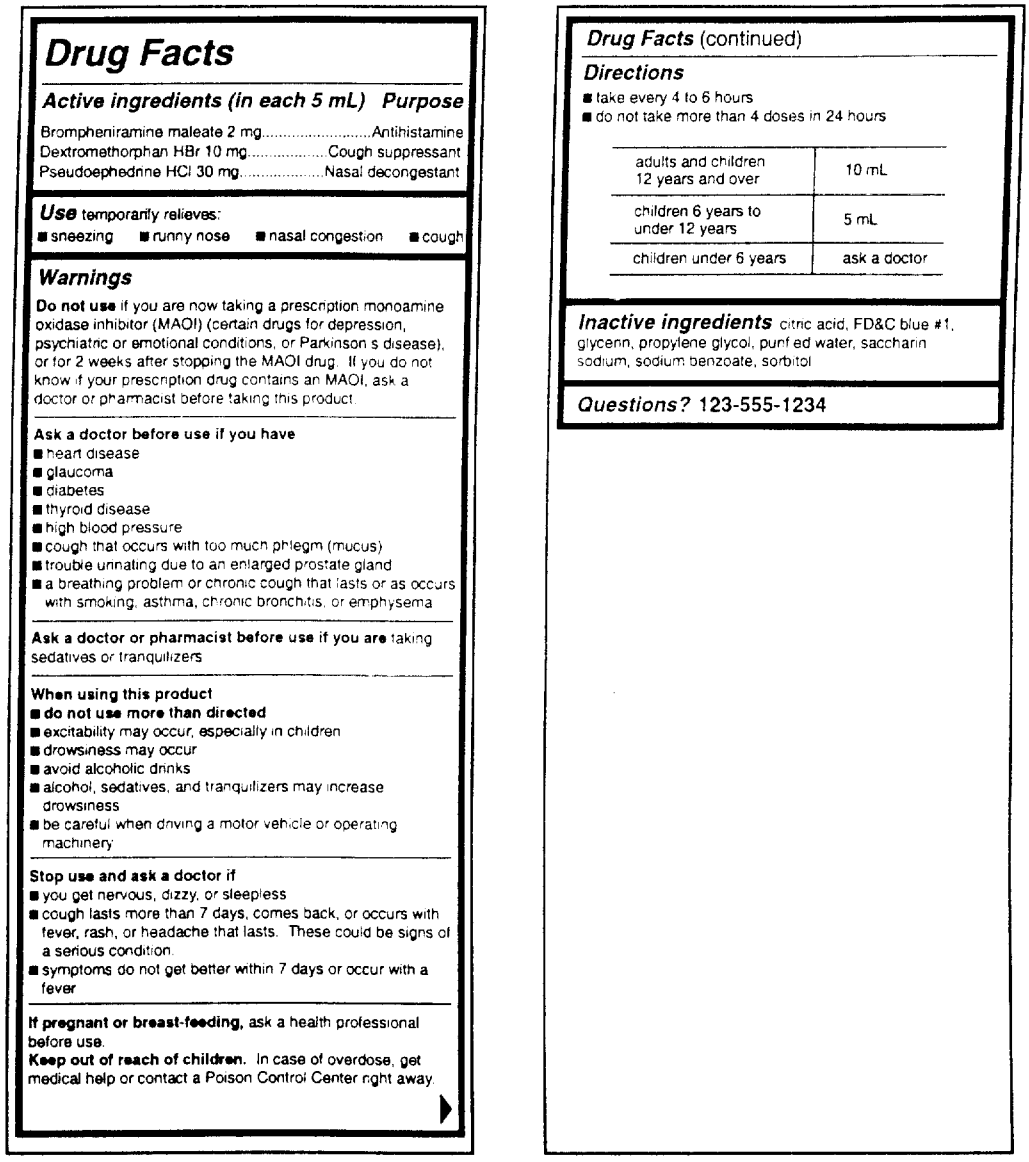
Other information ■ store at 20-25°C (68-77°F) ■ protect from excessive moisture

Inactive ingredients D&C yellow no. 10, lactose, magnesium stearate, microcrystalline cellulose, pregelatinized starch

* Note: 14 point Helvetica Bold Italic Title
8 point Helvetica Bold Italic Headings
6 point Helvetica Bold Subheadings
6 point Helvetica Regular Text
6.5 point Leading

Example 2

Combination Product Using Standard Labeling Format*
[Outer Carton]



Drug Facts

Active ingredients (in each 5 mL) Purpose

Brompheniramine maleate 2 mg.....Antihistamine
Dextromethorphan HBr 10 mg.....Cough suppressant
Pseudoephedrine HCl 30 mg.....Nasal decongestant

Use temporarily relieves:
■ sneezing ■ runny nose ■ nasal congestion ■ cough

Warnings

Do not use if you are now taking a prescription monoamine oxidase inhibitor (MAOI) (certain drugs for depression, psychiatric or emotional conditions, or Parkinson s disease), or for 2 weeks after stopping the MAOI drug. If you do not know if your prescription drug contains an MAOI, ask a doctor or pharmacist before taking this product.

Ask a doctor before use if you have
■ heart disease
■ glaucoma
■ diabetes
■ thyroid disease
■ high blood pressure
■ cough that occurs with too much phlegm (mucus)
■ trouble urinating due to an enlarged prostate gland
■ a breathing problem or chronic cough that lasts or as occurs with smoking, asthma, chronic bronchitis, or emphysema

Ask a doctor or pharmacist before use if you are taking sedatives or tranquilizers

When using this product
■ **do not use more than directed**
■ excitability may occur, especially in children
■ drowsiness may occur
■ avoid alcoholic drinks
■ alcohol, sedatives, and tranquilizers may increase drowsiness
■ be careful when driving a motor vehicle or operating machinery

Stop use and ask a doctor if
■ you get nervous, dizzy, or sleepless
■ cough lasts more than 7 days, comes back, or occurs with fever, rash, or headache that lasts. These could be signs of a serious condition.
■ symptoms do not get better within 7 days or occur with a fever

If pregnant or breast-feeding, ask a health professional before use.
Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.

Drug Facts (continued)

Directions
■ take every 4 to 6 hours
■ do not take more than 4 doses in 24 hours

adults and children 12 years and over	10 mL
children 6 years to under 12 years	5 mL
children under 6 years	ask a doctor

Inactive ingredients citric acid, FD&C blue #1, glycerin, propylene glycol, purified water, saccharin sodium, sodium benzoate, sorbitol

Questions? 123-555-1234

* Note: 14 point Helvetica Bold Italic Title
8 point Helvetica Bold Italic Headings
6 point Helvetica Bold Subheadings
6 point Helvetica Regular Text
8 point Helvetica Bold Telephone Number
7 point Leading

Example 3

Combination Product Using Section 201.66(d)(10) Modified Format*
[Bottle with Wraparound Label, No Outer Carton]

PDP Space

Drug Facts

Active ingredients (in each 5 mL)	***Purpose***
Brompheniramine maleate 2 mg	Antihistamine
Dextromethorphan HBr 10 mg	Cough suppressant
Pseudoephedrine HCl 30 mg	Nasal decongestant

Use temporarily relieves:
- sneezing
- runny nose
- nasal congestion
- cough

Warnings

Do not use if you are now taking a prescription monoamine oxidase inhibitor (MAOI) (certain drugs for depression, psychiatric or emotional conditions, or Parkinson's disease), or for 2 weeks after stopping the MAOI drug. If you do not know if your prescription drug contains an MAOI, ask a doctor or pharmacist before taking this product.

Ask a doctor before use if you have
- diabetes
- glaucoma
- thyroid disease
- cough that occurs with too much phlegm (mucus)
- trouble urinating due to an enlarged prostate gland
- heart disease
- a breathing problem or chronic cough that lasts or as occurs with smoking, asthma, chronic bronchitis, or emphysema
- high blood pressure

Ask a doctor or pharmacist before use if you are taking sedatives or tranquilizers

When using this product
- **do not use more than directed**
- drowsiness may occur
- avoid alcoholic drinks
- alcohol, sedatives, and tranquilizers may increase drowsiness
- be careful when driving a motor vehicle or operating machinery
- excitability may occur, especially in children

Stop use and ask a doctor if
- you get nervous, dizzy, or sleepless
- cough lasts more than 7 days, comes back, or occurs with fever, rash, or headache that lasts. These could be signs of a serious condition.
- symptoms do not get better within 7 days or occur with a fever

If pregnant or breast-feeding, ask a health professional before use.
Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.

Directions ■ take every 4 to 6 hours; not more than 4 doses in 24 hours

12 years and over	10 mL
6 to 12 years	5 mL
under 6 years	ask a doctor

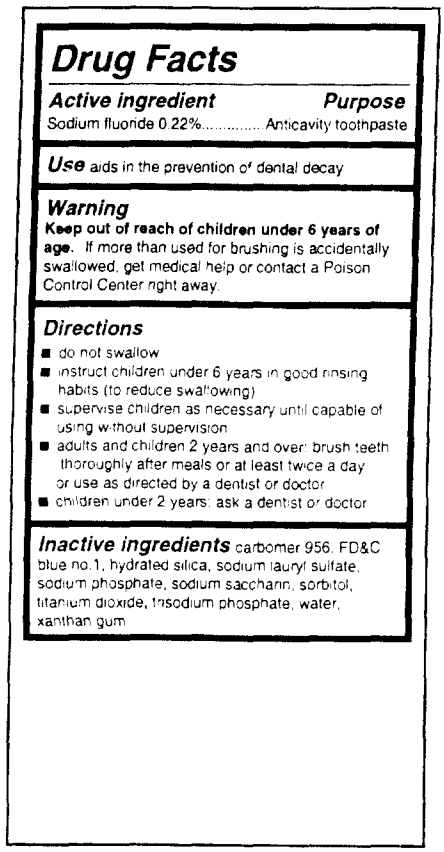
Inactive ingredients citric acid, FD&C blue #1, glycerin, propylene glycol, purified water, saccharin sodium, sodium benzoate, sorbitol

* Note: 12 point Helvetica Bold Italic Title
8 point Helvetica Bold Italic Headings
6 point Helvetica Bold Subheadings
6 point Helvetica Regular Text
6.5 point Leading

Box barline omitted; color contrast used to highlight Drug Facts information

Example 4

Product Using Standard Labeling Format*
[Stand Alone Tube, No Outer Carton]



Drug Facts

Active ingredient — **Purpose**

Sodium fluoride 0.22%..... Anticavity toothpaste

Use aids in the prevention of dental decay

Warning

Keep out of reach of children under 6 years of age. If more than used for brushing is accidentally swallowed, get medical help or contact a Poison Control Center right away.

Directions

- do not swallow
- instruct children under 6 years in good rinsing habits (to reduce swallowing)
- supervise children as necessary until capable of using without supervision
- adults and children 2 years and over: brush teeth thoroughly after meals or at least twice a day or use as directed by a dentist or doctor
- children under 2 years: ask a dentist or doctor

Inactive ingredients carbomer 956, FD&C blue no.1, hydrated silica, sodium lauryl sulfate, sodium phosphate, sodium saccharin, sorbitol, titanium dioxide, trisodium phosphate, water, xanthan gum

* Note: 14 point Helvetica Bold Italic Title
8 point Helvetica Bold Italic Headings
6 point Helvetica Bold Italic Subheadings
6 point Helvetica Regular Text
7 point Leading

Example 5

Drug-Cosmetic Product Using Standard Labeling Format*
[Irregular Shape Bottle Label, No Outer Carton]

Drug Facts

Active ingredient ***Purpose***
Selenium sulfide 1% .....Antidandruff

Use controls scalp itching and flaking due to dandruff

Warnings

For external use only

Ask a doctor before use if you have
- seborrheic dermatitis that covers a large area of the body

When using this product
- do not get into eyes. If contact occurs, rinse eyes thoroughly with water

Stop use and ask a doctor if
- condition worsens or does not improve after regular use

Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away

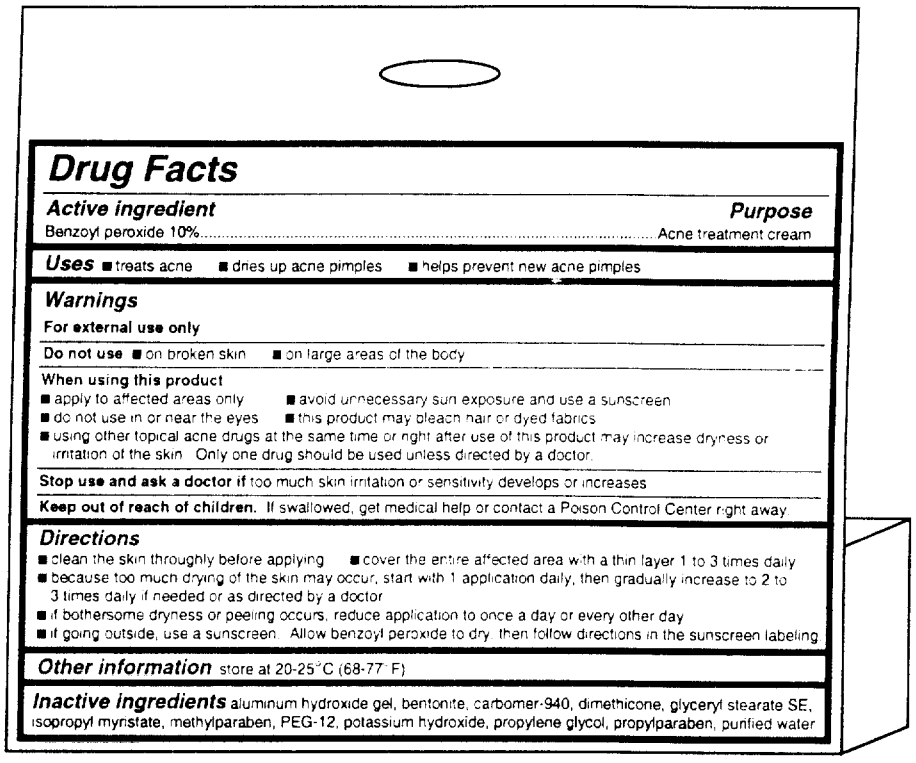
Directions
- shake well
- for best results, use at least 2 times a week

Inactive ingredients water, ammonium laureth sulfate, ammonium lauryl sulfate, cocamide MEA, glycol distearate, ammonium xylenesulfonate, dimethicone, tricetylmonium chloride, cetyl alcohol, DMDM hydantoin, sodium chloride, stearyl alcohol, hydroxypropyl methylcellulose, FD&C red no. 4

* Note: 14 point Helvetica Bold Italic Title
8 point Helvetica Bold Italic Headings
6 point Helvetica Bold Subheadings
6 point Helvetica Regular Text
7 point Leading

Example 6

Product Marketed In A Tube Using Standard Labeling Format*
[Packaged In A Carton Riser]



Drug Facts

Active ingredient — **Purpose**

Benzoyl peroxide 10% ..... Acne treatment cream

Uses ■ treats acne ■ dries up acne pimples ■ helps prevent new acne pimples

Warnings

For external use only

Do not use ■ on broken skin ■ on large areas of the body

When using this product

■ apply to affected areas only ■ avoid unnecessary sun exposure and use a sunscreen
■ do not use in or near the eyes ■ this product may bleach hair or dyed fabrics
■ using other topical acne drugs at the same time or right after use of this product may increase dryness or irritation of the skin. Only one drug should be used unless directed by a doctor.

Stop use and ask a doctor if too much skin irritation or sensitivity develops or increases

Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away.

Directions

■ clean the skin throughly before applying ■ cover the entire affected area with a thin layer 1 to 3 times daily
■ because too much drying of the skin may occur, start with 1 application daily, then gradually increase to 2 to 3 times daily if needed or as directed by a doctor
■ if bothersome dryness or peeling occurs, reduce application to once a day or every other day
■ if going outside, use a sunscreen. Allow benzoyl peroxide to dry, then follow directions in the sunscreen labeling.

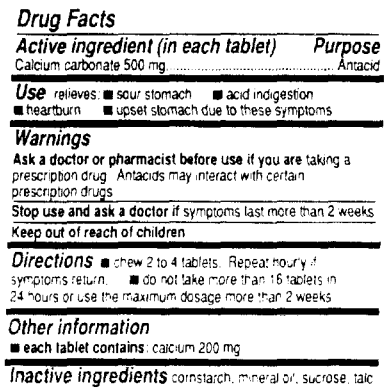
Other information store at 20-25°C (68-77°F)

Inactive ingredients aluminum hydroxide gel, bentonite, carbomer-940, dimethicone, glyceryl stearate SE, isopropyl myristate, methylparaben, PEG-12, potassium hydroxide, propylene glycol, propylparaben, purified water

* Note: 14 point Helvetica Bold Italic Title
8 point Helvetica Bold Italic Headings
6 point Helvetica Bold Subheadings
6 point Helvetica Regular Text
7 point Leading

Example 7

Product Using Section 201.66(d)(10) Modified Format*
[Tube With Wraparound Label]



Drug Facts

Active ingredient (in each tablet) ***Purpose***
Calcium carbonate 500 mg ..... Antacid

Use relieves: ■ sour stomach ■ acid indigestion ■ heartburn ■ upset stomach due to these symptoms

Warnings

Ask a doctor or pharmacist before use if you are taking a prescription drug. Antacids may interact with certain prescription drugs

Stop use and ask a doctor if symptoms last more than 2 weeks

Keep out of reach of children

Directions ■ chew 2 to 4 tablets. Repeat hourly if symptoms return. ■ do not take more than 16 tablets in 24 hours or use the maximum dosage more than 2 weeks

Other information

■ **each tablet contains**: calcium 200 mg

Inactive ingredients cornstarch, mineral oil, sucrose, talc

* Note: 9 point Helvetica Narrow Bold Italic Title
8 point Helvetica Narrow Bold Italic Headings
6 point Helvetica Narrow Bold Subheadings
6 point Helvetica Narrow Text
6 point Leading

therefore believes that while 4.5 point type may be appropriate in exceptional cases for nutritional information on a dietary supplement product, it is not an appropriate minimum type size for OTC drug products.

The agency recognizes the delicate balance between: (1) The need for the required information to fit within customary labeling and packaging constraints, and (2) the need to ensure that the required information is prominent and readable under customary conditions of purchase and use. The agency believes it has selected type sizes and styles that are consistent with the need for readable OTC drug product labeling by a majority of OTC drug consumers, while at the same time taking into account the manner in which OTC products are marketed and the economic impact posed by setting these minimum requirements (see section VIII of this document).

24. Some comments suggested a sliding scale for type size based on package size, similar to the requirements for dietary supplements and food labeling (§§ 101.9(j)(13) and 101.36(j)(2)). The agency generally supports the ap formatting for products marketed in p to develop such an approach for OTC of package sizes for OTC drug produ Therefore, the agency has focused in for typical OTC drug products. Never point size wherever the package may has specified in § 201.66(d)(2) the rel a larger type size is used for the required text.

The agency notes that san serif type styles have been adopted by at least one trade association as the industry standard. The agency believes that san serif type styles are the most likely to be considered clear and easy-to-read.

3. Font, Leading, Kerning, Contrast, and Highlighting (§ 201.66(d)(3))

Section 201.66(d)(3) contains font, leading, kerning, contrast, and highlighting requirements. The agency has determined that at least 0.5-point leading (i.e., the space between two lines of text) is needed to ensure readability. While the proposal would have limited type style to Helvetica, the final rule will allow any single clear sans serif, easy-to-read, type style. The agency also is requiring

and because letter compression is an important factor in determining readability, the agency is requiring that all type be presented using no more than 39 characters per inch.

the title ''Drug Facts'' and the ''Drug Facts'' part of the ''Drug Facts (continued)'' title to appear in bold italic print to draw even more attention to the required information panel and, thereby, contribute to the goal of ensuring that consumers are appropriately signaled to read and use the information which follows. The agency is requiring the type to be all black or one dark color, ~~and it can be~~ printed on a white or other light, neutral color, contrasting background.

25. Several comments requested that the agency allow the use of any sans serif type style in OTC drug product labeling. The agency is allowing any single, ~~sans serif~~ clear, easy-to-read, type style, ~~with no more than 39 characters per inch~~ because ~~sans serif~~ font styles vary in their stroke weight characteristics (i.e., the thickness of the character of each letter is variable). ~~These variations make some more readable than others.~~ Because Helvetica and Univers font styles in particular have consistent and uniform stroke weight characteristics and are both commonly available, the agency therefore recommends the use of ~~either~~ one of these font styles.

26. Several comments requested that only the format layout should be required and not the graphical features (i.e., type size, leading, kerning, and highlighting). If graphical features are required, the comments requested reduced type size and leading.

Based on the discussion in the proposed rule (62 FR 9024 at 9036), the agency has determined that both format layout and graphical features are necessary to ensure that labeling information is conveyed in a manner that enables the consumer to readily notice and comprehend such information. The agency has revised the leading requirement from the proposed 1-point leading to 0.5-point leading in this final rule.

4. Bullets (§ 201.66(d)(4))

Section 201.66(d)(4) specifies the style and format for using bullet points to introduce and highlight statements of information. The bullet style is limited to solid squares or solid circles of 5-point type size and must be presented in the same shape and color throughout the labeling. The use of a solid circle or square will avoid selection of an icon that may have an independent meaning, such as an octagon (stop) or inverted triangle (caution). This format provides a valuable

(including the PDP); or (2) where more than 60 percent of the total surface area available for labeling on the back and side panels must be used to satisfy the ''content requirements'' in proposed § 201.66(c); or (3) that is a trial size package, packet, or single use unit. Some comments proposed that any drug or drug-cosmetic product that meets this definition be exempt from the new format and content requirements, but should still bear all required labeling. Some comments stated that a performance standard, as described in the proposed rule (62 FR 9024 at 9036), has not been established or validated and would be impractical to use for small packages at this time.

The agency agrees that some manufacturers may have difficulty providing important drug information, which is prominent and easy to read, on packages that are irregular (i.e., bottle labels) or small (i.e., unit does). However, the agency also considers the required OTC drug labeling information essential for the safe and effective use of OTC drug products, irrespective of the size or the shape of the package.

Because readability is especially dependent on vertical letter height and letter compression, the agency disagrees that less than 6-point type or letter compression allowing more than 39 characters per inch should be permitted (Ref. 11), even on ''small packages.'' As discussed in response to comment 23 in section IV.D of this document, the agency considers 6.0 type the minimum allowable for OTC drug product labeling.

The agency, however, is including in § 201.66(d)(10) of this final rule several modifications that may be used with packages that are too small to meet the format requirements of paragraphs (d)(1) through (d)(9). Under § 201.66(d)(10), the leading may be adjusted so that the ascenders and descenders of the letters do not touch, rather than the 0.5-point leading required under § 201.66(d)(3). The box or similar enclosure required in § 201.66(d)(8) may be omitted if the headings, subheadings, and information in § 201.66(c)(1) through (c)(9) are set off from the rest of the label by color contrast ~~(i.e., type shall be all black or one dark color type, printed on a white or other light neutral color contrasting background).~~

The agency, however, is including in § 201.66(d)(10) of this final rule several modifications that may be used with packages that are too small to meet the format requirements of paragraphs (d)(1) through (d)(9). Under § 201.66(d)(10), the leading may be adjusted so that the ascenders and descenders of the letters do not touch, rather than the 0.5-point leading required under § 201.66(d)(3). Also, bulleted statements may continue to the next line of text and need not be vertically aligned. Finally, the box or similar enclosure required in § 201.66(d)(8) may be omitted if the headings, subheadings, and information in § 201.66(c)(1) through (c)(9) are set off from the rest of the label by color contrast.

As suggested by the comments, a product will be considered "small," and will be permitted to apply these modifications, if more than 60 percent of the total surface area available to bear labeling on the entire outside container or wrapper, or the immediate container label if there is no outside container or wrapper, would be needed to present FDA required labeling. This consists of the labeling required by § 201.66(c)(1) through (c)(9), in accordance with the minimum specifications in § 201.66(d)(1) through (d)(9), ~~and the tamper evident statement, expiration date, lot or control number, and name and place of business of the manufacturer, packer, or distributor, as provided in 21 CFR 201.1~~) This formula is consistent with the idea that 40 percent of available labeling space is generally reserved for the UPC symbol and a PDP (see, e.g., 21 CFR 101.1 and § 201.60 (21 CFR 201.60)).

and any other FDA required information for drug products and, as appropriate, cosmetic products; other than information required to appear on a principle display panel.

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number of OTC drug

Section 201.66(e) in this final rule provides that FDA, on its own initiative, or in response to a written request from any manufacturer, packer, or distributor, may exempt or defer, based on the particular circumstances presented, one or more specific requirements set forth in § 201.66(a) through (d), on the basis that the requirement is inapplicable, impracticable, or would be contrary to public health or safety.

The agency agrees that the exemption process need not require a citizen petition. However, the process should be a matter of public record and requests for exemptions must be granted by the agency prior to marketing. Requests for exemptions must be submitted in three copies in the form of an ''Application for Exemption'' to the agency. The requests shall be clearly identified on the envelope as a ''Request for Exemption from 21 CFR 201.66 (OTC Labeling Format)'' and with Docket No. 98N–0337. A separate request must be submitted for each OTC drug product. In addition to the three copies of the exemption request submitted to the agency, manufacturers of a product marketed under an approved drug application must also submit a single copy of the exemption request to their application. Decisions on exemptions and deferrals will be maintained in a permanent file in this docket for public review.

The request for exemption or deferral must: (1) Document why a particular requirement is inapplicable, ~~cannot be achieved~~ impracticable, or would be contrary to public health or safety, and (2) include a representation of the proposed label and labeling, including outserts, panel extensions, or other graphical or packaging intended to be used with the product.

35. In the proposed rule, the agency asked for comment on whether there are particular types of products or packages that should be granted a regulatory exemption (62 FR 9024 at 9038). At least one comment, from a trade association, requested that ''drug-cosmetic products,'' and particularly those that do not have a dosage limitation (e.g., antidandruff shampoos, anticaries toothpastes, antiperspirants, and sunscreens), be exempted from the new labeling requirements. The comment argued that these products do not raise serious adverse event concerns, are not used to treat serious health problems, do not raise serious misuse concerns, do not have the potential

in formulation (and purpose) of many combination OTC drug products so that medication errors can be avoided and consumers can appropriately self-select an OTC drug product for their condition(s).

The agency also emphasizes that with drug-cosmetic products, self-selection is very important because consumers often must choose between a cosmetic or a drug-cosmetic product. A consumer who has dandruff should select an antidandruff-conditioner shampoo rather than a conditioner shampoo; a consumer who wishes to prevent sunburn should select a sunscreen-moisturizer rather than a moisturizer; a consumer who perspires heavily should select an antiperspirant-deodorant rather than a deodorant; a consumer who needs to prevent caries should select a fluoride toothpaste rather than a nonfluoride toothpaste. This final rule provides a format for presenting information that will allow consumers to readily distinguish among seemingly similar products and to readily access important drug information.

The agency agrees that there may be limited instances in which a labeling requirement may discourage manufacturers from marketing certain products for a drug use (e.g., lipsticks containing sunscreens or lip balms containing skin protectant ingredients). These products, when they contain an ingredient intended to provide a therapeutic effect, do provide significant public health benefits to consumers.

When developing drug labeling, the agency considers the risks and benefits of ~~a~~ the drug, the intended use, and the need to communicate limitations or restrictions about ~~use~~ the use of the product to the target population. The quantity and complexity of information which must be communicated to ensure appropriate product selection, convey the effectiveness of the drug, communicate risks, and provide complete directions for use, varies with the drug ingredient, the target population, the disease or symptoms the product is intended to treat or prevent, and ~~with~~ related information about the conditions which must be provided for the safe and effective use of the drug.

In some cases (e.g., lipsticks or lip balms containing sunscreen), minimal information is needed for the safe and effective use of the product. Such products may typically be packaged in small amounts, have

a ~~very~~ high therapeutic index, carry extremely low risk in actual consumer use situations, provide a favorable public health benefit, require no specified dosage limitation, and require few specific warnings and no general warnings (e.g., pregnancy or overdose warnings). ~~Products that meet these characteristics will be identified, addressed, and specifically considered for exemptions in their respective monographs and drug marketing applications.~~

36. One comment noted that OTC

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The agency will identify products with these characteristics and will consider appropriate exemptions in their respective monographs and drug marketing applications. In addition, under new §201.66(e), FDA, on its own initiative, or in response to a written request from any manufacturer, packer, or distributer, may exempt or defer one or more specific requirements set forth in §201.66 (a) through (d).

d

presents a

FDA exempt OTC drug

labeling requirements.

The agency disagrees with these comments. As discussed, sound public policy and the dictates of the act require that drug-cosmetic products present readable, understandable, prominent, and conspicuous drug labeling. With respect to export issues, section 802 of the act (21 U.S.C. 382) sets forth those instances in which exported drug products are not required to be labeled in accordance with the requirements for domestic marketing. The agency notes that an OTC drug product exported in accordance with section 802 of the act would not be required to meet labeling requirements for domestic marketing (such as the requirements imposed by this rule), except to the extent that the import country itself has adopted U.S. requirements (see section 802(b)(1) and (f) of the act).

F. Interchangeable and Connecting Terms (§§ 201.66(f) and 330.1(i) and (j))

Section 201.66(f) permits specific terms codified in § 330.1(i) (''interchangeable terms'') to be used interchangeably in the labeling of OTC drug products, provided such use does not alter the meaning of labeling established in an applicable OTC drug monograph or regulation. Section

8-point or greater type, or 2-point sizes greater than the point size of the text. The letter height or type size for the subheadings and all other information described in paragraphs (c)(2) through (c)(9) of this section shall be no smaller than 6-point type.

(3) The title, headings, subheadings, and information in paragraphs (c)(1) through (c)(9) of this section shall be legible and clearly presented, shall not appear in reverse type, shall have at least 0.5-point leading (i.e., space between two lines of text), and shall not have letters that touch. The type style for the title, headings, subheadings, and all other required information described in paragraphs (c)(2) through (c)(9) of this section shall be any single, Clear ~~sans serif~~, easy-to-read type style, with no more than 39 characters per inch. The title and headings shall be in bold italic, and the subheadings shall be in bold type, except that the word ''(continued)'' in the title ''Drug Facts (continued)'' shall be regular type. The type shall be all black or one dark color, printed on a white or other light, neutral color, contrasting background, except that the title and the headings may be presented in a single, alternative, contrasting dark color unless otherwise provided in an approved drug application, OTC drug monograph (e.g., current requirements for bold print in §§ 341.76 and 341.80 of this chapter), or other OTC drug regulation (e.g., the requirement for a box and red letters in § 201.308(c)(1)).

(4) When there is more than one statement, each individual statement listed under the headings and subheadings in paragraphs (c)(4) through (c)(7) of this section shall be preceded by a solid square or solid circle bullet of 5-point type size. Bullets shall be presented in the same shape and color throughout the labeling. If more than one bulleted statement is placed on the same horizontal line, the end of one bulleted statement shall be separated from the beginning of the next bulleted statement by at least two square ''ems'' (i.e., two squares of the size of the letter ''M'') and the complete additional bulleted statement(s) shall not continue onto the next line of text. All bullets under a heading or subheading shall be vertically aligned.

(5) The title, headings, subheadings, and information set forth in paragraphs (c)(1) through (c)(9) of this section may appear on more than one panel on the outside container of the retail

the ''Drug Facts (continued)'' title, a horizontal hairline shall follow the title and immediately precede the heading. A horizontal hairline extending within two spaces on either side of the ''Drug Facts'' box or similar enclosure shall immediately follow the title and shall immediately precede each of the subheadings set forth in paragraph (c)(5) of this section, except the subheadings in paragraphs (c)(5)(ii)(A) through (c)(5)(ii)(G) of this section.

(9) The information set forth in paragraph (c)(6) of this section under the heading ''Directions'' shall appear in a table format when dosage directions are provided for three or more age groups or populations. The last line of the table may be the horizontal barline immediately preceding the heading of the next section of the labeling.

(10) If the title, headings, subheadings, and information in paragraphs (c)(1) through (c)(9) of this section, printed in accordance with the specifications in paragraphs (d)(1) through (d)(9) of this section, ~~and the tamper evident statement, expiration date, lot or control number, and name of the manufacturer, packer, or distributor,~~ require more than 60 percent of the total surface area available to bear labeling, then the Drug Facts labeling shall be printed in accordance with the specifications set forth in paragraphs (d)(10)(i) through (d)(10)(iv) of this section. In determining whether more than 60 percent of the total surface area available to bear labeling is required, the indications for use listed under the ''Use(s)'' heading, as set forth in paragraph (c)(4) of this section, shall be limited to the minimum required uses reflected in the applicable monograph, as provided in § 330.1(c)(2) of this chapter.

and any other FDA required information for drug products, and, as appropriate, cosmetic products, other than information required ~~by FDA~~ to appear on a principle display panel,

(i) Paragraphs (d)(1), (d)(2), (d)(5

(ii) Paragraph (d)(3) of this sectio
be used, provided the ascenders and de

(iii) Paragraph (d)(4) of this sectic
is placed on the same horizontal line, t
line of text, and except that the bullets
aligned.

available to bear labeling, then the Drug Facts labeling shall be printed in accordance with the specifications set forth in paragraphs (d)(10)(i) through (d)(10)(iv) of this section. In determining whether more than 60 percent of the total surface area available to bear labeling is required, the indications for use listed under the ''Use(s)'' heading, as set forth in paragraph (c)(4) of this section, shall be limited to the minimum required uses reflected in the applicable monograph, as provided in § 330.1(c)(2) of this chapter.

(i) Paragraphs (d)(1), (d)(2), (d)(5), (d)(6), and (d)(7) of this section shall apply.

(ii) Paragraph (d)(3) of this section shall apply except that less than 0.5-point leading may be used, provided the ascenders and descenders do not touch.

(iii) Paragraph (d)(4) of this section shall apply except that if more than one bulleted statement is placed on the same horizontal line, the additional bulleted statements may continue to the next line of text, and except that the bullets under each heading or subheading need not be vertically aligned.

(iv) Paragraph (d)(8) of this section shall apply except that the box or similar enclosure required in paragraph (d)(8) may be omitted if the Drug Facts labeling is set off from the rest of the labeling by use of color contrast (i.e., type shall be all black or one dark color type, printed on a white or other light neutral color contrasting background).

(11)(i) The following labeling outlines the various provisions in paragraphs (c) and (d) of this section:

Insert 5
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(ii) Paragraph (d)(2) of this section shall apply except that the letter height or type size for the title "Drug Facts (continued)" shall be no smaller than 7-point type and the headings in paragraphs (c)(2) through (c)(9) of this section shall be the larger of either 7-point or greater type, or 1-point size greater than the point size of the text.

Examples of

Appendix A to Part 201—Graphic Enhancements Used by FDA

Graphic Enhancements

I. Section 201.66 Standard Labeling Format

A. Overall

1. The ''Drug Facts'' labeling is set off in a box or similar enclosure by the use of a barline with all black type printed on a white, color contrasting background.

B. Typeface and size

1. ''Drug Facts'' is set in 14 point Helvetica Bold Italic, left justified.

2. ''Drug Facts (continued)'' is set in 8 point Helvetica Bold Italic for the words ''Drug Facts'' and 8 point Helvetica Regular for the word ''(continued)'' and is left justified.

3. The headings (e.g., ''Directions'') are set in 8 point Helvetica Bold Italic, left justified.

4. The subheadings (e.g., ''Ask a doctor or pharmacist before use if you are'') are set in 6 point Helvetica Bold, left justified.

5. The information is set in 6 point Helvetica Regular with 6.5 point leading, left justified.

6. The heading ''Purpose'' is right justified.

7. The bullet is a 5 point solid square.

8. Two em spacing separates bullets when more than one bullet is on the same line.

9. A table format is used for 3 or more dosage directions.

10. A graphic appears at the bottom of the first panel leading the reader to the next panel.

C. Barlines and hairlines

1. A 2.5-point horizontal barline extends to each end of the ''Drug Facts'' box (or similar enclosure), providing separation between each of the headings.

2. A 0.5-point horizontal hairline extends within 2 spaces on either side of the ''Drug Facts'' box (or similar enclosure), immediately following the title and immediately preceding the subheadings.

3. A 0.5-point horizontal hairline follows the title, immediately preceding the heading, when a heading appears on a subsequent panel immediately after the ''Drug Facts (continued)'' title.

D. Box or Enclosure

1. All information is enclosed by a 2.5-point barline.

II. Section 201.66 Modified Labeling Format

A. Overall

1. The ''Drug Facts'' labeling is presented with in all black type printed on a white color contrasting background.

B. Typeface and size

1. ''Drug Facts'' is set in 9 point Helvetica Bold Italic, left justified.

2. The headings (e.g., ''Directions'') are set in 8 point Helvetica Bold Italic, left justified.

3. The subheadings (e.g., ''Ask a doctor or pharmacist before use if you are'') are set in 6 point Helvetica Bold, left justified.

4. The information is set in 6 point Helvetica Regular with 6.5 point leading, left justified.

5. The heading ''Purpose'' is right justified.

6. The bullet is a 5 point solid square.

7. Bulleted information may start on same line as headings (except for the ''Warnings'' heading) and subheadings, with 2 em spacing separating bullets, and need not be vertically aligned.

C. Barlines and hairlines

1. A 2.5-point horizontal barline extends to each end of the ''Drug Facts'' box (or similar enclosure), providing separation between each of the headings.

2. A 0.5-point horizontal hairline extends within 2 spaces on either side of the ''Drug Facts'' box (or similar enclosure), immediately following the title and immediately preceding the subheadings.

D. Box or Enclosure

1. All information is set off by color contrast. No barline is used.

CROSS FILE SHEET

FILE NO: 98N-0337 | REF1

SEE FILE NO: 96N-0420 / REF1
95N-0259 / REF1
90P-0201 / REF2